"The roof of the mouth is beefsteak red, and beefy and has a white exudate on it There are deep furrows The same picture is present on the sides of the cheeks and on the uvula The pharynx is red and 'angry looking' There is one small lesion on the gum over the left upper incisor"

An oral surgeon called in consultation stated The patient appears to have an inflammatory hyperplasia of the oral mucosa, very marked on the palate, with fissures I saw the patient at the suggestion of Dr John G Downing, who had seen the previous patient (case 2) at a meeting of the New England Dermatological Society and suggested that this patient probably had pyostomatitis vegetans The following is my consultation note

"Examination of the oral cavity shows a soft verrucous eruption of the hard and soft palate mucosa extending downward to include the uvula The mucosa of both cheeks shows folding in the molar regions but no active process at the present time Minute pinpoint whitish abscesses can be demonstrated in the lesions of the soft palate and uvula There are a few miliary abscesses in the upper part of the vestibule of the mouth in the cuspid regions The tongue shows an area of denudation of the coating, probably due to contact irritation from lesion of the palate The picture is strongly suggestive of a condition known as pyostomatitis vegetans"

Following is the report on the biopsy specimen taken from the palatal region of an old verrucous lesion

"The epithelial surface shows moderate hyperkeratosis and marked acanthosis with broadening of the rete pegs The underlying tunica propria shows a marked dense cellular infiltration with disorganization of the collagen fibers There is moderately increased capillary vascularization The cellular infiltration is very pronounced in the subepithelial zone and the papillas and extends into the epithelial surface forming dense collections of cells made up principally of lymphoid and plasma cells There is spongiosis of the acanthotic epithelium with many infiltrating lymphocytes extending to the surface epithelial layer The cellular infiltrate in the tunica propria is pleomorphic, with plasma cells predominating and relatively few polymorphonuclear leukocytes An occasional multinucleated cell is seen, and only a rare eosinophil is demonstrated The picture is that of a granulomatous inflammatory process of a chronic type The relative absence of eosinophils in this case as compared to the marked eosinophilia seen in early lesions can be explained by the age of the lesions The clinical picture together with the histologic findings indicates a chronic granulomatous process involving the oral cavity Two other cases of pyostomatitis previously seen by me differ only in that in more acute lesions the eosinophils predominate in the cellular exudate The diagnosis is pyostomatitis vegetans"

A report from the family physician received in November 1948 stated that there had been an improvement in the oral condition a year ago but that he had not seen the patient since that time

CLINICAL DESCRIPTION AND COURSE OF ORAL LESIONS

There was a remarkable similarity in the clinical courses in all 3 cases In cases 1 and 3 the disease was confined to the mouth throughout its entire course, and an opportunity to observe the primary lesions was presented in case 1 owing to a recent relapse after the mouth had been normal for three and one-half months

intraepidermal cavity with numerous eosinophils In the upper cutis the vessels are dilated and show swelling of the intima There is a diffuse infiltration of small round cells, wandering connective tissue cells, numerous eosinophils and occasional plasma cells"

Treatment has consisted of superficial irradiation, injections of arsenic and liver extract and blood and plasma transfusions Sulfapyridine was given, but its use had to be discontinued because of nausea and vomiting The last treatment given in the hospital and being continued in the clinic is administration of

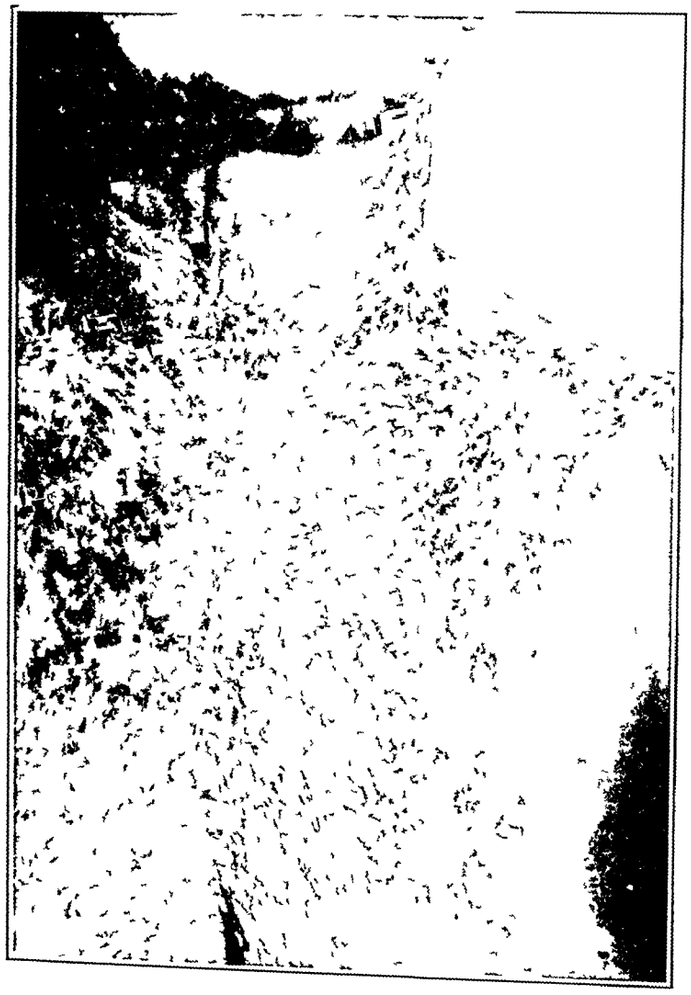


Fig 1—Vesicular eruption on neck and chest in a woman with questionable dermatitis herpetiformis

naphuride® in a dose of 0 25 Gm intramuscularly twice a week This seems to have benefited the patient

DISCUSSION

Dr Francis A Ellis, Baltimore Nausea is not a contraindication to the administration of sulfapyridine We have had severe cases in which we continued to use the drug in spite of nausea and vomiting, and even though the dosage was decreased, good results were obtained in three or four weeks

The primary lesions of pyostomatitis vegetans are noted as flat minute miliary abscesses on a slightly raised dark red inflammatory base The abscesses are uniform in size, suggesting early miliary tubercles, and tend to be more or less conglomerate, about 2 to 3 mm apart The process spreads within a very few weeks to involve the whole mouth, including the mucosa of the cheeks, the vestibule, the gingivas, the lingual aspects of the lips, the hard and soft palates and, to a limited degree, the margins of the tongue

As the condition develops chronically, the buccal mucosa begins to proliferate, is thrown into folds and assumes a verrucous appearance The miliary abscesses persist as fixed lesions and are found on the summits of the rugae and in the deep invaginations The mucosa is swollen, red and soft to palpation Under the dental plate in case 2 the miliary abscesses tended to rupture, leaving erosions with an accumulation of exudate becoming sticky from admixture with saliva This exudate could be peeled off, especially in the morning after inspissation from mouth breathing Smears from the miliary abscesses in the early stages show up to 30 per cent eosinophils and the remainder polymorphonuclear leukocytes

Only mild subjective symptoms occurred in each case, and the swollen verrucous lesions were not tender to the touch The verrucous mucosa acted as an insulating surface, and the ingestion of hot or spicy foods was not associated with any unusual discomfort In each case the course was relatively benign and of unusual chronicity with only slight periods of remission

The lesions of the oral mucous membrane were very distinctive and not simulated by those of any other oral disease

Although not a direct etiologic factor, the chronic diarrhea in 2 cases played an important role in lowering the resistance of both patients Both patients could be considered as below normal in their general health, and both had had recent acute infections, in case 2 the oral eruption appeared just after the attack of diarrhea had cleared up

The improvement in the oral disease in both cases was related to the use of liver and iron, together with prolonged vacations, rather than to any local treatment to the mouth

The cutaneous lesions in case 2 suggested an inoculation from the primary lesions in the mouth, but this was not proved The rapid spread of the vegetating cutaneous lesion of the groin was very striking and gave the clinical appearance of blastomycosis cutis The histologic picture was essentially the same as in the specimens removed from the mouth When the patient was hospitalized after three months of local treatment, the cutaneous condition responded to local antiseptic



Fig 1—Lesions of chronic discoid lupus erythematosus on the face



Fig 2—Lesions of chronic discoid lupus erythematosus in the upper half of the tattooed red heart on the left arm

treatment together with radiation therapy There has been no recurrence of the cutaneous lesions in case 2 after several months, although a residual palatal process still persists

It was the cutaneous eruption in case 2 which made it possible finally to clarify the diagnosis of the oral disease in all the cases

BACTERIOLOGY

Smears and cultures from the oral cavity were taken in all cases and also from the cutaneous lesion in case 2 The following report was submitted by Dr Ralph Wheeler, Department of Bacteriology, Tufts College Medical and Dental Schools

CASE 1—Fresh unstained preparations showed numerous pus cells, desquamated epithelial cells, a few red cells and no amebas The dark field was negative for spirochetes Smears showed gram-negative diplococci and short bacilli as the predominating organisms A few gram-positive diplococci were seen, but acid-fast organisms were not demonstrated Wright stain showed 11 per cent eosinophils, but no Leishman-Donovan bodies Vincent's organisms were not found. Cultures on blood agar plates and anaerobic cultures showed a variety of organisms consistent with the normal oral flora, the predominating micro-organisms being gram-negative diplococci, gram-positive micrococci, nonhemolytic enterococci, streptococci of the viridans group and a single colony of aerobic actinomycetes, probably a normal inhabitant

CASE 2—Essentially the same general bacterial flora was found as in case 1 A long gram-negative filamentous organism was found but not identified Saliva filtrate inoculated into the allantoic membrane of chick embryo produced no growth Cultures from the miliary abscesses from the lesion of the skin of the groin showed Staph aureus with a few colonies of hemolytic streptococci

CASE 3—The cultures from the lesions in the oral cavity showed the predominant organism to be a streptococcus of the viridans group There were no beta hemolytic streptococci found on culture

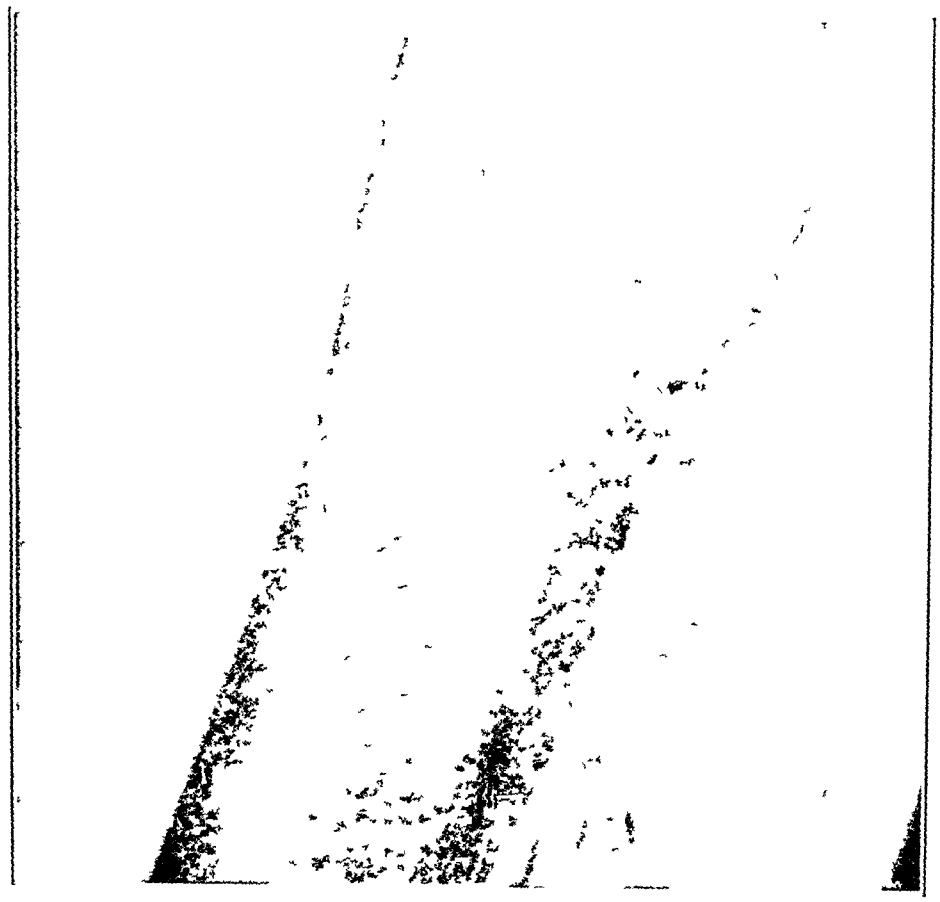
It can be concluded that these findings, together with the clinical course of the disease, indicate that the oral and cutaneous manifestations are not related to the micro-organisms demonstrated

PATHOLOGY OF ORAL AND CUTANEOUS LESIONS

Six biopsies in all were made from the oral lesions in all cases and one from the verrucous lesion of the skin in case 2

The general histologic pictures observed in these specimens were essentially the same The cutaneous lesions showed more pronounced hyperkeratosis with more extreme acanthosis and developed deeper invaginations of the surface epithelial layer. There was a more pronounced cellular infiltration with more numerous eosinophils in the upper part of the cutis and relatively larger miliary abscesses The oral lesions showed a marked acanthosis with broadening and elongation of the rete pegs with the epithelial surface thrown into folds, in places showing fairly deep invaginations Infiltrating eosinophil and poly-

of subcutaneous hemorrhage on both legs and thighs The oral mucous membranes were dry, and the submaxillary salivary glands were visibly enlarged, firm and of a rubbery consistency The parotid glands were affected similarly, but to a less degree Except for a slight hepatic enlargement and generalized superficial lymphadenopathy, the rest of the general physical examination showed no abnormality Examination with a slit lamp by the ophthalmologic consultant revealed many keratitic precipitates and deposits of pigment on the anterior capsule of the lens of each eye There were numerous clear grayish nodules on the anterior surface of the iris of each eye Moderate circumcorneal injection was present The ophthalomologic diagnosis was uveitis due to sarcoidal involvement, a condition which, in combination with the parotid swelling, could be classified as Heerfordt's disease (uveoparotid fever)



Lesions on patient's arm

Roentgenologic study revealed a mottled density in the lower field of the left lung and bilateral enlargement of the hilar nodes Reactions to the Mantoux test were negative with dilutions of 1 10, 1 500, 1 1,000, 1 10,000 and 1 20,000 History of a positive cutaneous reaction to a tuberculin test four years previously was later obtained from the patient Repeated examinations of sputum, gastric washings and cultures revealed no tubercle bacilli Except for an increase of the sedimentation rate to 47 mm, routine studies of the blood and urine revealed nothing abnormal The plasma globulin level was slightly elevated Serologic tests for syphilis were negative, as was the intracutaneous reaction to Frei antigen (lygranum) Microscopic study of cutaneous biopsy specimens by Dr M R Caro revealed moderate hyperkeratosis of the epidermis, with attenuation of the rete pegs There were focal perivascular accumulations of large mononuclear

morphonuclear leukocytes were noted in the deeper epidermal epithelium A very striking and distinctive picture was the presence of epidermal miliary abscesses with the predominating cell the polymorphonuclear coarsely granular eosinophil leukocyte Focal areas showing epithelial thinning with necrosis at the site of rupture of miliary abscesses were present The tunica propria showed a very marked cellular infiltrate, chiefly eosinophilic, especially in the region of the papillae Deeper in the specimens the cellular infiltration was slight to moderate In addition to the cellular infiltration of the tunica propria, there was considerable edema with increased capillary vascularity Proliferation of the endothelium in the young blood vessels was noted

The over-all picture was that of a granulomatous inflammatory process with unruptured miliary epidermal abscesses and focal areas of surface necrosis The tissue and blood eosinophilia was striking in 2 cases, although not diagnostic, as eosinophilic infiltration of tissue lesions and the presence of eosinophils in the peripheral blood stream are commonly observed in pemphigus vegetans, dermatitis herpetiformis and other dermatoses

DIFFERENTIAL DIAGNOSIS

When first seen and for several months afterward the disease involving the oral cavity remained undiagnosed, and it was only after the characteristic verrucous lesion of the skin in case 2 developed that a definite diagnosis was made

In pemphigus vegetans, oral lesions are characterized by a primary flaccid bullous lesion which contains a serous fluid tinged with blood These bullae rupture early, leaving superficial painful eroded areas New lesions continue to form, and the oral condition presents a characteristic appearance Desquamated epithelium and a fibrinous exudate frequently coat the superficial ulcerations In very chronic oral involvement, focal areas of proliferating granulation tissue may develop but the process is very painful

In the very rare oral disease oral pemphigus, in which the lesions are confined to the mouth, the primary lesions are also bullous and the process may continue for years Extension to the pharynx may occur in these cases, and pain is a prominent symptom

Dermatitis herpetiformis has been described as a disease that may cause cutaneous lesions similar to those described in pemphigus vegetans Oral involvement in dermatitis herpetiformis has been described, with lesions essentially the same as in pemphigus vegetans However, many dermatologists state definitely that the mouth is not involved in this disease, and I have never seen a single case of dermatitis herpetiformis with oral lesions

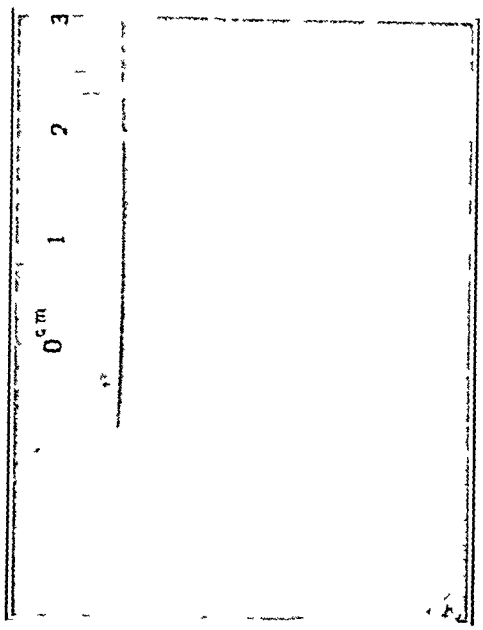


Fig 1—Nodular lesions in the cubital area appearing after an intravenous injection of calcium levulinate



Fig 2—Photomicrograph (× 100) showing foreign body tubercles with giant cells and deposits of calcium

Lupus erythematosus not infrequently shows buccal lesions which tend to ulcerate early and usually are associated with subjective symptoms of pain and soreness, although some patients are relatively free from pain The lesions are sharply defined and their appearance varies with the age of the lesion The common locations are on the lips and in the vestibule of the mouth, especially in the molar regions The palate and gingivas, together with other locations, may be involved The lesions in the beginning are bright red plaques with slightly infiltrated borders, with thinning of the centers as the lesions progress Many of these lesions as they heal resemble those of leukoplakia

Eosinophilic granuloma,[18] regarded by many as an entity, has in recent years been described in the dermatologic literature The complexity of the clinical picture and a more specific histologic picture help to differentiate this condition from the oral and cutaneous lesions of pyostomatitis vegetans To date there has been no mention of oral lesions in all the cases of eosinophilic granuloma reported in the literature

TREATMENT

As indicated in the description of these cases, local therapy had no effect in clearing up the lesions Local and parenteral administration of penicillin and oral administration of sulfonamide drugs had no beneficial effect on the mucosal lesions Use of iron and liver together with prolonged vacations was effective in aiding the return to normal of the buccal mucosa in case 1, and in case 2 a similar result was accomplished except for a residual process on the palate after twenty-two months In case 3, according to the most recent report, in 1947, there was improvement in the oral condition with a residual process still persisting in the palate region

SUMMARY

Three cases of a rare vegetating oral mucosal disease are described in 1 of which typical pyodermatitis vegetans developed, in the others the condition remained as an oral entity

Pyostomatitis vegetans presents a characteristic and distinctive oral disease with primary miliary abscesses on an inflammatory base with the development of verrucous changes

The clinical course in 2 cases was confined to the oral cavity, these are the only cases reported in the literature in which the disease remained an oral entity

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In case 2 a complicating vegetating dermatitis developed, the pathologic picture presenting the same changes as were found in the oral lesions in the 3 cases

The oral lesions were resistant to local oral therapy in all cases, but the cutaneous lesion responded to antiseptic and radiation therapy

Bacteriologic study of the oral lesions in all 3 cases revealed no specific micro-organisms or virus

A similarity to pemphigus vegetans is indicated, but the clinical course with characteristic oral lesions indicates a definite disease entity involving the oral cavity

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NONLIPID GRANULAR CELL TUMORS

HAROLD N COLE, M D
AND
HERBERT LUND, M D
In Collaboration with H N Cole Jr, M D, J R Driver, M D, Richard C Light, M D, and Don R Printz, M D
CLEVELAND

NONLIPID granular cell tumors are usually considered to be myoblastomas, and in the following review this term will be used freely However, identity of all these tumors is still open to question We present 3 cases exemplifying this problem

In 1926 Abrikossoff [1] reported a tumor of myoblasts occurring chiefly in relation to striated muscle He thought it might be due to degenerative lesions following injury or inflammation In 1931 [2] he further elaborated his ideas on myoblastic myomas, as he called them, feeling that perhaps they were made up of embryonal elements primitive myoblasts He divided them into four different types, of which the first three are all granular cell and benign (1) round, egg-shaped or elongated myoblasts, 20 to 25 microns in length, showing granules but no longitudinal or cross striations, (2) growths in which some of the cells may show longitudinal or cross striations, and (3) a hypertrophic form with cells 40 to 160 microns in length and at times multinucleated. He also described a further type (4), in which the myoblasts are not granular but atypical, which resembles more a polymorphous sarcoma

Crane and Tremblay,[3] in reporting 5 cases in 1945, pointed out that, although Abrikossoff had reported 5 cases in 1926, Weber in 1854, Hertaux in 1881, Pendel in 1897 and Moschcowitz in 1922 had described what were apparently identical lesions Crane and Tremblay reviewed

Read at the Sixty-Eighth Annual Meeting of the American Dermatological Association, Inc, San Diego, Calif, April 28, 1948

From the Department of Dermatology and Syphilology and from the Institute of Pathology of the Western Reserve University School of Medicine and of the University Hospitals

1 Abrikossoff, A Ueber Myome ausgehend von der quergestreiften willkurlichen Muskulatur, Virchows Arch f path Anat **260**·215-233, 1926

2 Abrikossoff, A I Weitere Untersuchungen uber Myoblastenmyome, Virchows Arch f path Anat **280** 723-740, 1931

3 Crane, A R, and Tremblay, R G Myoblastoma (Granular Cell Myoblastoma or Myoblastic Myoma), Am J Path **21**·357-375 (March) 1945

the literature, which up to the time of their publication consisted of 162 cases, 34 of the skin and subcutis and 61 of the tongue

In the past few years there has been much more interest directed to this group of tumors, with quite extensive reports, among others those by Klemperer,[4] Howe and Warren,[5] Ravich, Stout and Ravich,[6] Powell[7] and Khanolkar[8] Reports on the disease, as it has become better known, have mounted rapidly, thus Powell reported 4 cases in 1946, Simon,[9] 6 in 1947, Khanolkar, a further 10 in September 1947, and Allen,[10] 27 in 1948 The total, including Bloom and Ginzler's,[11] Cipollaro and Einhorn's[12] recent cases and our 3 cases, is around 214 cases It is our view that as the entity becomes better known and as the physician becomes more inclined to examine lesions histologically, granular cell myoblastoma will be found to be far from a rare entity Thus Allen found 27 myoblastomas in material from 8,000 specimens of cutaneous diseases collected in World War II by the Army Institute of Pathology

LOCALIZATION AND CHARACTERISTICS

These tumors seem to be found most frequently on the tongue and in the mouth and larynx, in about some 37 per cent of the cases The growths have been distributed all over the body and in some internal organs

Strangely enough, the occurrence of these tumors in the second most frequently involved area, the skin and subcutis, has not been sufficiently emphasized until in the very recent literature Powell in 1946 stated that 20 4 per cent of the cases so far reported had involved these structures In 3 of her 4 cases the cutaneous surfaces were affected—

4 Klemperer, P Myoblastomata of Striated Muscle, Am J Cancer **20** 324-337 (Feb) 1934

5 Howe, C W, and Warren, S Myoblastoma, Surgery **16** 319-347 (Sept) 1944

6 Ravich, A, Stout, A P, and Ravich, R A Malignant Granular Cell Myoblastoma Involving Urinary Bladder, Ann Surg **121** 361-372 (March) 1945

7 Powell, E B Granular Cell Myoblastoma, Arch Path **42** 517-524 (Nov) 1946

8 Khanolkar, V R Granular Cell Myoblastoma, Am J Path **23** 721-739 (Sept) 1947

9 Simon, M A Granular Cell Myoblastoma, Am J Clin Path **17** 302-313 (April) 1947

10 Allen, A C Survey of Pathologic Studies of Cutaneous Diseases During World War II, Arch Dermat & Syph **57** 19-56 (Jan) 1948

11 Bloom, D, and Ginzler, A M Myoblastoma, Arch Dermat & Syph **56** 648-658 (Nov) 1947

12 Cipollaro, A C, and Einhorn, M B Granular Cell Myoblastoma, Arch Dermat & Syph **56** 812-818 (Dec) 1947

in 1 with multiple lesions Tuta and Schmidt[13] in 1942 reported 3 examples of cutaneous involvement and 1 of the trapezius muscle Ebert and Slepyan[14] the next year presented a patient before the Chicago Dermatological Society with a small nodule on the dorsum of the left hand In the discussion Becker[15] stated that he had recently seen in consultation with Dr Clarence Shaw a similar tumor on the upper part of the chest Then Bloom and Ginzler reported the case of a Negro woman with a hazelnut-sized, round, raised tumor of the lip which, after endothermy, was followed two years later by a hazelnut-sized nodule of the skin and subcutis of the right thigh, a similar lesion on the trunk and a smaller one on the right hip Very recently Cipollaro and Einhorn observed a marble-sized nodule of the right index finger as well as one on the tongue There have been a few instances reported of polyp-like masses in the ear canals, which growths may attract attention by bleeding

These tumors are very often symptomless, are many times sessile and vary in size from 0 5 to 2 0 or 3 0 cm , occasionally being even larger Their color on the mucous membrane is often described as grayish or opalescent In Ebert and Slepyan's case the quarter-sized mass was made up of several smaller nodules Rarely are the growths painful unless in a vital structure and ulcerating as well The patients vary from newborn babes with small lesions of the alveolar processes up to persons in the second, third or fourth decade of life, rarely older

MICROSCOPIC APPEARANCE

These tumors are generally well circumscribed, ovoid or lobulated and rather firm Occasionally the borders may show outlying islands of cells and may even penetrate surrounding tissues The growths are made up of rather large, elongated or polyhedral cells, appearing as single cells or in sheets They may have a banjo or tadpole shape or the shape of a tear drop, as has been mentioned by many writers And some tumors will show a striking pseudoacinar appearance of the cells They have a coarse, granular cytoplasm, acidophilic in character, and nuclei that are comparatively small and have an angular appearance In some cases the cells may be multinucleated The cytoplasm is often foamy, resembling somewhat that of a xanthoma cell However, it does not have the tinctorial reactions of the latter Occasionally the cells

13 Tuta, J A , and Schmidt, F R So-Called Myoblastoma, Arch Dermat & Syph **46** 225-233 (Aug) 1942

14 Ebert, M H , and Slepyan, A H So-Called Myoblastoma, Arch Dermat & Syph **48** 348-349 (Sept) 1943

15 Becker, S W , in discussion on Ebert and Slepyan[14]

in certain tumors will show suggestions of longitudinal or cross striations Keynes [16] and Klemperer pointed out the interesting feature of overgrowth of the overlying epithelium where the skin or mucous membrane is concerned—a pseudoepitheliomatous hyperplasia This condition was striking in the cases of Bloom and Ginzler, even to the production of pearls, which the pathologists interpreted as indicative of a low grade squamous cell carcinoma

MALIGNANT GRANULAR CELL TUMORS

Originally, Abrikossoff separated a fourth group of tumors resembling more a polymorphous sarcoma, which is quite generally not included in the classification of granular cell myoblastomas Howe and Warren reported that they had seen 10 cases, among which there were 5 with definite malignant properties, 3 of the growths metastasizing to the lung They also stated that they had found 10 cases in the literature and 4 of their own with either gross or microscopic evidence of local invasion There had been regional adenopathy in 7 cases, but in only 3 were metastases to lymph nodes proved by biopsy In none was there response to irradiation Ravich, Stout and Ravich expressed the opinion that all 5 of their cases should be put in Abrikossoff's fourth class They were skeptical of the malignant character of this tumor until the occurrence of their own case, in which a tumor of the bladder recurred after excision and in which the patient died eleven months later from metastases They stated the belief that their case is the first example of a type 3 tumor metastasizing and causing death However, in Morpurgo's [17] case the patient, with a tumor of the tongue, died with metastases in the cervical nodes In Powell's patient 3, who had a large growth in the floor of the mouth, displacing the tongue, there was invasion of the tissues and death from erosion of a vessel Moreover, in her case 4 there were tumors in the scalp, the upper eyelid, the lower lip, the right axilla, the right side of the torso, the left thigh, the vulva, the back, the toe and the buttock, as well as of the uterus and an ovary After removal of some of these, including the uterine and ovarian growths, further growths developed on the skin This development of further cutaneous lesions also occurred in Bloom and Ginzler's case after partial removal of the tumor of the lip Moreover, Khanolkar, in a recent article, reported a further 10 cases in which there could be no uncertainty regarding the neoplastic nature These

16 Keynes, G Rhabdomyoma of Tongue, Brit J Surg **13** 570-572 (Jan) 1926

17 Morpurgo, B Myoblastomi, Arch per le sc med **59** 229-252 (Feb) 1935, cited by Bloom and Ginzler [11]

data, we think, force one to believe that at times granular cell myoblastoma may be malignant Ewing[18] expressed the opinion that most myoblastomas are benign

ORIGIN

Originally the theory was evolved that these tumors were degenerative lesions following injury or inflammation or that they arose from embryonal muscle cells Gray and Gruenfeld[19] stated the belief that the evidence for the theory is insufficient except for the tongue tumors The frequent appearance of the growths on the tongue has suggested the possibility of trauma This possibility was also suggested in Khanolkar's case 1, which followed a fall Crane and Tremblay in 1945 stated that "Definite statement as to the histiogenesis of these tumors is probably unwise at this time" Perhaps this opinion represents good judgment for the present

TREATMENT

As to their treatment, practically all authors agree that these tumors are not amenable to radiotherapy If they are recognized, it would seem to be good judgment for one to excise them, widely, if possible Otherwise, it would be well, if possible, for one to excise the growth and cauterize the base, if the lesion is small

The information concerning these tumors certainly suggests to dermatologists and surgeons the more frequent adoption of biopsy, otherwise many of them will not be recognized

CASE 1—N M, aged 71, a retired Naval officer, was admitted with the complaint of a sore on the tongue, of three weeks' duration

The patient had been a heavy pipe smoker for many years and had but recently noticed this spot on the tongue He did not remember having bitten himself

Physical examination revealed on the left side of the tongue, about halfway back and slightly toward the ventral aspect, a small, somewhat indurated, pearly white lesion, about 6 mm in diameter The area was slightly tender

With the use of local anesthesia the entire lesion was widely excised for biopsy and the base thoroughly destroyed with electrocautery The patient has been followed for two years and shows no evidence of recurrence of the lesion

The histologic report stated that the paraffin section stained with hematoxylin and eosin included buccal mucosa, a zone of atypical cells and underlying skeletal muscle The mucosa was hyperplastic, and irregular pegs extended deeply There was keratinization of groups of the deeper cells The cells were mature Mitoses in the epithelium were rare There was slight parakeratosis Pseudoepitheliomatous proliferation was striking

18 Ewing, J Neoplastic Diseases A Treatise on Tumors, ed 4, Philadelphia, W B Saunders Company, 1940

19 Gray, S H, and Gruenfeld, G E Myoblastoma, Am J Cancer **30** 699-708 (Aug) 1937

Atypical cells extended from the inferior border of the epithelium, with which they were in immediate contact, to the underlying skeletal muscle They formed a broad sheet within which were occasional slender septums of connective tissue cells and capillaries Deeply, they mingle with the muscle fibers There were groups consisting in part of striated muscle fibers and in part of atypical cells The diameter of the atypical cells was larger than that of the muscle fibers, but these cells had the same general shape and had sharply outlined boundaries The cytoplasm was pale and finely granular and occasionally contained acidophilic clumps, in some instances they formed fine, parallel, linear, closely arranged, fibrillar lines Cross striation was not identified The nuclei were small but



Fig 1 (case 1) —Myoblastoma of the tongue, with pseudoepitheliomatous hyperplasia of mucosa, × 86

tended to be larger and more rounded than those of normal striated muscle They showed faint, weblike chromatin and, occasionally, a pale pink dot resembling a nucleolus Mitoses were not seen The atypical cells appeared to extend beyond the deep margin of excision

A frozen section showed no sudanophilic droplets in the cells

CASE 2—V B, a Negro woman aged 41, was first seen in April 1946, complaining of a small lump on the left side of her tongue The mass had been first noticed one year previously, was asymptomatic and had been slowly enlarging

The history, except for that of syphilis, which had been well treated, was not relevant

On the left lateral border of the tongue, midway between the tip and the base, was a well defined, very firm, nontender tumor This measured 0 8 by 0 7 by 0 5 cm, was almost white and had a rough, somewhat verrucous surface Other oral mucosae were normal, but the teeth were extensively carious



Fig 2 (case 2)—Myoblastoma of the tongue, superficial part of tumor, with pseudoepitheliomatous hyperplasia, × 86

The entire lesion was widely excised and the base thoroughly cauterized Eighteen months later the patient was entirely cured

Histologic examination revealed this section to be almost identical with that for case 1 The atypical cells had the same distribution and appearance It was noted that some cells showed a mixture of appearances, in part resembling normal sarcoplasm At the periphery or at one side the cytoplasm might be

brightly eosinophilic and compact, as in normal striated muscle cells, while centrally or at an opposite side it was loose, pale and granular Cells of intermediate intensity of staining were also present They had loose fibrils and faint cross striations and resembled skeletal muscle except that they were larger and paler No mitoses were present The atypical cells extended to the depth of the section The epidermis was similar in every respect to the section from case 1



Fig 3 (case 2) —Myoblastoma, deep portion of tumor, in which may be seen mixture of the granular cells with the striated muscle of the tongue, × 134

There was more parakeratosis, however, and an extreme pseudoepitheliomatous hyperplasia

CASE 3[20]—L S, a man aged 40, had had a gradually developing tumor in the anteropalmar aspect of the distal phalanx of the right thumb for four years

20 Included through the courtesy of Dr J M Hamilton and of Dr D J Rehbock, clinical pathologist, St Vincent Charity Hospital

The tumor was freely movable and completely painless There was a history of catching the thumb in a door jamb and pinching it severely some months before In fact, the injury had been so severe that the patient had only a spoon nail on that digit. His occupation was not relevant

The tumor was only recently excised through an incision of the skin without removal of skin There were no other lesions

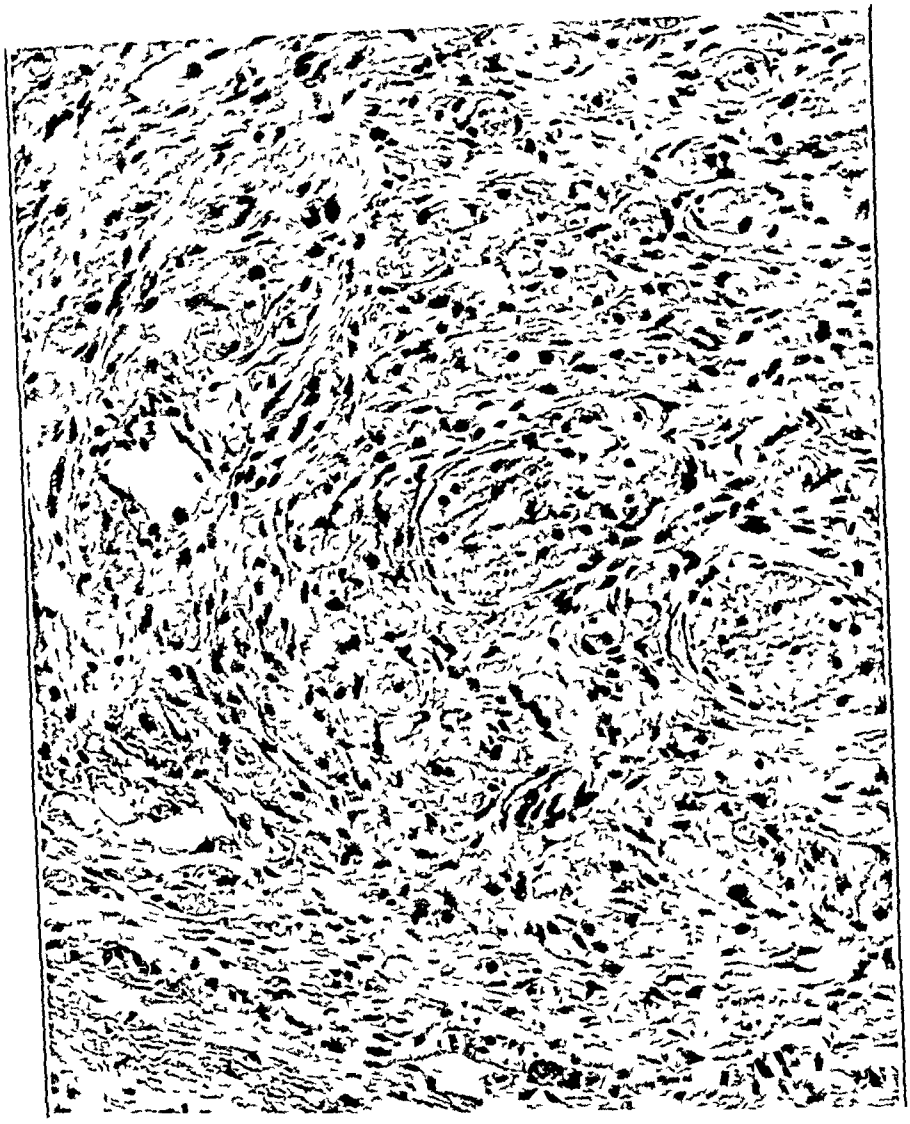


Fig 4 (case 3) —Granular cell tumor of finger, with coarse granularity of cells, about × 200

The specimen consisted of an ovoid, firm, pearly gray tissue mass, measuring 1 0 by 0 6 cm The surface was lobulated but otherwise smooth Section revealed a firm, fibrous, pearly gray tissue

The paraffin section stained with hematoxylin and eosin consisted largely of rounded groups of atypical cells enclosed by a circle of fusiform cells and hyaline fibers These groups were in turn collected and held together by interlacing bands of hyaline fibers, and the entire mass was bounded by collagenous tissue on two sides Outside of this capsule were a little areolar tissue and a few sweat glands The other two sides were cut surfaces

The atypical cells were round and polyhedral or long and cylindric They were granular and moderately eosinophilic The granules were fine, although a few coarse hyaline clumps were seen Indistinct cross markings were seen Some of these appeared as very fine basophilic lines, and others had an appearance produced by parallel arrangement of granules Some nuclei were basophilic, compact and small Others were larger and showed a reticular and punctate chromatin pattern Single or multiple nuclei might be seen in a single cell Where cells were longitudinally cut, spaced nuclei might be seen in a row Mitoses were not present

COMMENT

In the two lingual lesions there were transitions from striated muscular cells to granular atypical cells (fig 3) It is reasonable to conclude that for these the term myoblastoma is justified

In case 3, however, there were differences The cells were larger and more coarsely granular, and there was grouping in round nests, in contrast to the uniform sheets found in the lingual lesions Muscular relations were not seen Further, the tumor arose in a site away from normally situated skeletal muscle The histologic diagnoses entertained were myoblastoma, traumatic pseudoneuroma and neurofibroma The first-mentioned one seemed the most likely

At this juncture the presentation of Fust and Custer [21] concerning granular cell neurofibroma was heard, and the slide was sent to them for an opinion They expressed the opinion that it was an example of granular cell neurofibroma

Without further study concerning the nature of these tumors, and pending the publication of Fust and Custer's work, we choose to call the lesion a granular cell tumor and to be noncommittal concerning its origin

SUMMARY

A report is made of 2 cases of granular cell myoblastoma of the tongue and of a subcutaneous granular cell tumor of the thumb They are discussed from a clinical and microscopic standpoint

Such tumors are probably much commoner than is suspected

The tumors are found most frequently on the tongue and in the mouth and appendages, they are seen next most frequently on the skin and subcutis

While in most cases these tumors are not malignant, nevertheless sufficient reports are accumulating to indicate that in certain locations and under certain conditions invasion, metastases and death may result from less than total surgical removal The tumors are highly radioresistant

21 Fust, J A, and Custer, R P The Neurogenesis of So-Called Granular Cell Myoblastoma, Am J Clin Path **19** 522-535 (June) 1949

There are a few cases in which these growths have been multiple in type on the skin and subcutis as well as in internal organs

In tumors of the skin and mucous membrane, the pseudoepithelioma-tous hyperplasia is frequent enough to be noteworthy

The tumors of the tongue strongly suggest muscular origin Other tumors without demonstrable transition from or location in muscular tissue are more obscure The work of Fust and Custer is anticipated

1352 Hanna Building (15)
2085 Adelbert Road (6)

ABSTRACT OF DISCUSSION

Dr Hamilton Montgomery, Rochester, Minn I have been interested in myoblastoma ever since Dr Machacek called my attention to this condition several years ago when the American Academy of Dermatology met in New York A fellow in pathology at the Mayo Clinic, Dr G H Murphy, just finished studying 10 cases which he classified under the headings of the uniform type of myoblastoma, which is benign, and the pleomorphic type, which is essentially a rhabdomyosarcoma The granular cells appear in both types I had formerly accepted the concept that granular cell myoblastoma arose from skeletal muscles Recently, however, I have seen 2 cases in which there apparently was origin from smooth muscles In 1 case there was a lesion on the vulva of a Negro woman aged 72, which showed smooth muscle origin Material from a recent case with involvement of the anal region, sent to me by Dr Wasserman of Cincinnati, showed granular myoblastoma cells apparently arising in relation to the walls of the capillaries in the papillary bodies This observation would suggest endothelial origin, because these capillaries are not supposed to have a muscular coat In some of Murphy's cases of the pleomorphic type, there was a history of trauma preceding the development of the tumor and subsequent metastasis and death Myoblastoma does not have a typical clinical appearance but does have a characteristic histologic one

Dr Anthony Cipollaro, New York My attention was brought to this disease several years ago when a patient came to my office with a small lesion on the tongue I diagnosed it as a fibroma I was going to infiltrate it with procaine hydrochloride (novocain®) and destroy it with electrodesiccation, but, because the man was worried about cancer, I removed the tissue and submitted it for biopsy The type of lesion was not recognized by the first dermatopathologist It had unusual cells with which I was not familiar Dr Richter, a general pathologist, immediately diagnosed it as a granular cell myoblastoma This case was published by me a few months ago in the Archives [12]

I think that all nodular lesions of the tongue should be removed and submitted to the laboratory for histologic study

Dr. Louis Winer, Hollywood, Calif Recently my associates and I had submitted to our laboratory a piece of tissue which showed myoblastoma The differential stains were very interesting Van Gieson stain colored the blastoma tissues yellow, like smooth muscles Mallory's stain showed the tissue to be bright red, just as it does muscle fibers Therefore, I would advise that differential staining be done In the case of neurofibromatosis, also, differential stains would be of benefit because the tissue in neurofibromatous structure is mostly fibrous and stains like connective tissue, red with Van Gieson and greenish blue with Mallory's stain

DR HARRY ARNOLD JR, Honolulu, Hawaii I should like to mention in this connection an instance of a small lesion on the side of a young woman's neck, clinically an obvious granuloma pyogenicum, which was sectioned in our laboratory purely as a routine matter and turned out to be an infiltrating, anaplastic, granular cell carcinoma, the cells of which were full of fat It was an example of the sort of lesion Dr Cipollaro spoke of, which is all too frequently merely thrown away after its removal Excision of the operative site the following afternoon revealed a nest of residual neoplasm

DR HAROLD N COLE, Cleveland Thank you all for the discussion I mentioned a classification of these tumors containing four groups The fourth group is that of a nongranular polymorphic sarcoma, generally not accepted as a granular cell myoblastoma, and should be deleted

USE OF REPELLENTS IN CLINICAL DERMATOLOGY

General Principles

LEON GOLDMAN, M D
CINCINNATI

AMONG the advances in preventive medicine in the last world war were the detailed studies in the chemical control of insects As yet, the practicing physician, as compared with the military physician does not appear to be fully aware of the possibilities for the control of insects, especially the disease-bearing types This chemical control, in general, falls into two phases insecticidal and repellent activity

The development of insecticides is well known from the advances in the preparations of pyrethrins and DDT (2,2-bis [p-chlorophenyl]-1,1,1-trichloroethane) and its newer analogues, such as DDD (1,1-dichloro-2,2-bis-[p-chlorophenyl]-ethane) and methoxychlor (1,1,1-trichloro-2,2-bis [p-methoxyphenyl]-ethane Perhaps less is known about the developments of new insecticidal materials, which include such substances as gammexane® (hexachlorocyclohexane), velsicol 1068® (also called chlordan), hexaethyltetraphosphate, piperine compounds, parathion (0,0-diethyl-0-p-nitrophenyl thiophosphate), very toxic, phenyl cellosolve® (ethylene glycol monophenyl ether) and eura® (10 per cent crotonyl-N-ethyl-ortho-toluidide) [1] Dermatologists should be interested also in the development of effective modern rodenticides, such as 1080, alpha-naphthyl-thiourea, and fanyline

Repellents have a distinct and important value because they serve, by means of a protective cloud of volatile products about the person, by taste mechanisms, by physical or mechanical means, etc, to keep insects away Repellents are necessary, for it may be possible for one to be bitten during the latent period of activity of an insecticide At present, it is not possible to combine in a single universally effective mixture both insecticidal and repellent properties Prior to World War I, few, if any, effective repellent materials were available Smokes and oil of citronella were old favorites During World War II thousands of compounds [2] were tested, and continued to be tested, for their repellent and toxic qualities against mosquitoes, lice, mites, ticks and "other

From the Department of Dermatology and Syphilology of the University of Cincinnati College of Medicine

1 Heyroth, F Personal communications to the author

2 Travis, M, and Cochran Insect Repellents Used as Skin Treatment by the Armed Forces, J Econ Entomol **39** 637, 1946, Chem Abst, vol 41, no 2207

arthropods affecting the health of man" [3] The brilliant researches of the various governmental groups are especially known by the studies on DDT However, equally important work has been done, and continues to be done, especially by the Bureau of Entomology and Plant Quarantine of the Agricultural Research Administration, in the investigation of repellents Effective mixtures, well known to military physicians, were the dimethylphthalate solutions and the dimethylphthalate combined with hexanediol and indalone® (butyl ester of 3,4-dihydro-2,2-dimethyl-4-oxo-1,2-pyran-6-carboxylic acid) Toward the end of the war, Pijoan [1] and Jachowski,[1] working at the Naval Medical Research Institute, developed the NMRI-448 repellent This compound represents the four hundred and forty-eighth attempt to find an effective repellent mixture, which essentially was the combination of 70 per cent 2-phenylcyclohexanol and 30 per cent 2-cyclohexylcyclohexanol Jachowski [1] claimed that NMRI-448 is superior to the 612 and the 622 mixture in effectiveness against the mosquitoes of tropical America and of equal effectiveness against the mosquitoes of the United States and Alaska Recent work has indicated that N-propyl-N,N-diethylsuccinamate has also good repellent action when applied to the skin Recent work by Brennan [3] has also included the development, especially as a repellent for ticks (Dermacentor andersoni, Amblyomma americanum), of phenylcyclohexanol and butylacetanilide Our preliminary studies with N,n-butylacetanilide indicate that this material is also of low sensitivity index

With regard to the protection of the person, the two significant features of repellent activity are, first, the limitation of the protection to the area or areas to which the repellent has been applied and, second, the duration of activity of the repellent action In general, the repellent mixture in a suitable vehicle may be used locally on the skin, or clothing may be impregnated with it The duration of the activity varies with the type of repellent, and perhaps with the type of vehicle The recent development in the use of repellents has increased the time of repellent activity to approximately eight hours for the NMRI-448 group Clothing impregnation prolongs the period of repellent activity Against ticks, the repellent activity is said to last as long as twelve days

Repellents in dermatologic practice are useful specifically in preventing chigger infestation and bites, mosquito bites, fly bites and flea bites, they act as a tick repellent and possibly are of value in management of the familial infestations pediculosis and scabies

Protective clothing and various types of sulfur preparations have been used to prevent chigger (genus Trombicula) infestations In

3 Brennan, J M Preliminary Report on Some Organic Materials as Tick Repellents and Toxic Agents, Pub Health Rep **62** 1162, 1947

recent years, I have used benzyl benzoate preparations on the lower extremities as a protective measure King has indicated that for uniform impregnation against chiggers these five new compounds are all superior to benzyl benzoate, benzyl, 2-thenyl benzoate, p-cresyl benzoate, diphenyl carbonate and 2-thenyl salicylate The modern repellent for the prevention of chigger bites are rubbed in from the ankle to the knee, they are also put into the cuffs of trousers, clothing may be impregnated and the substance rubbed into shoes The technic of this application refers to protection of the person only while he is walking through chigger-infested areas, for sitting or lying in the grass, however, greater areas of the body must be protected Besides the usual severe discomfort from these bites, significant reactions may occur in the elderly, in persons with latent and actual stasis syndromes and in infants and young children with extensive bites Parkhurst [1] emphasized repeatedly the necessity of preventing bites from the chigger For the use of repellents against flying insects, such as flies and fleas, the repellent must be used on the exposed areas of the skin Such areas include chiefly the head, neck, neck line, wrists, arms and trouser line It should be remembered that the repellent must be reapplied if the supposed period of activity has been exceeded When repellents are mixed in "sun tan mixtures," one must consider the possible insect-attracting qualities of these mixtures

For those insects which serve as vectors for disease, such as ticks, mosquitoes, simulia and flies of the Phlebotomus group, these repellents have an importance far beyond the prevention of the mere initial cutaneous bite In a previous report,[4] the relation of the lichen urticatus syndrome in children to bites from insects was shown For those children, repellents are needed, especially against fleas, chiggers and bedbugs Tick repellents also may be applied to the skin or the clothing impregnated Although repellents should have value in familial infestations with Phthirus pubis, Pediculus capitis and Sarcoptes scabiei, few controlled studies on civilian groups are available In practice, actual antiparasiticidal treatment of the entire family, especially in the case of scabies (scabies domestica), is carried out, and the repellents, though less irritating, are not needed

The mixtures of repellents that were developed by the armed services during the war have undergone, in addition to severe critical laboratory use and field trials, controlled tests with regard to systemic

4 Goldman, L Lichen Urticatus Syndrome as a Manifestation of Sensitivity to Bites from Various Species of Arthropods, Arch Dermat & Syph **58** 74 (July) 1948 Draize, J H , Nelson, A A , and Calvery, H O The Percutaneous Absorption of DDT (2,2-Bis [p-Chlorophenyl] 1,1,1-Trichlorethane) in Laboratory Animals, J Pharmacol & Exper Therap **82** 159, 1944

toxicity and cutaneous irritation and sensitivity As an example, to develop a technic of screen testing for rapid elimination of those compounds which would be harmful to man and animals, Draize, Nelson and Calvery [4] devised a detailed percutaneous toxicity test on animals The materials that are available now, as a result of such extensive cooperative work, are mixtures with a low sensitivity index

From experience, it appears that the discomfort suffered with the use of repellents is usually caused by its vehicles, alcohol or other solvents, rather than by the repellents themselves It is the solvent that is responsible for the burning around the eyes and mouth and on active sunburned areas For some time cream vehicles, with a content of liquid repellent varying from 10 to 60 per cent, have been suggested by the Orlando Florida Laboratory of the Bureau of Entomology and Plant Quarantine of the Agricultural Research Administration In general, a cream type of vehicle is preferable

Persons traveling to tropical or subtropical areas should receive, in addition to their protective inoculations, simple and practical instructions regarding the modern uses of insecticides and repellents The dermatologic aspects of modern insecticides will be reported in another article

CONCLUSION

Greater use should be made by the civilian dermatologist of the recent advances in the chemical control of insects Repellents are of value for the prevention of bites, especially in the case of persons who are sensitive to bites of the mosquito, fly, flea, chigger (Trombicula) and the tick Persons traveling in foreign countries and in tropical or subtropical areas should be instructed in the chemical control of insects This instruction is as important as the detailed inoculation program The activity of the repellent is limited to the area or areas protected and by its duration Repellents may be used in liquid or in cream form, or the clothing may be impregnated The repellents available now are materials of low sensitivity index

University of Cincinnati

Clinical Notes

PROGRESSIVE DISSEMINATED COCCIDIOIDOMYCOSIS

WERNER W DUEMLING, M D
SAN DIEGO, CALIF

In 1892 Wernicke[1] and Posada[2] reported the first known case of coccidioidal granuloma Two years later Rixford[3] described the first case in the American literature At that time the causative agent was considered to be a protozoan, because of the resemblance of the indolent ulcers of the skin in this disease to those produced in animals by coccidia, the name of coccidioides was suggested for this agent In 1900 Ophuls[4] recognized and described the causative agent as a moldlike parasite which was readily cultured on various mediums It has been within the last decade that valley fever, the syndrome of influenza and erythema nodosum, has been attributed to coccidioides[5] This recognition of the primary infection has caused a considerable change in attitude toward the disease Coccidioidal infection, once considered a rarity when recognized only in the granulomatous stage, is now not uncommon, however, the extensive and unusual involvement in the following cases which came under our observation merits reporting in detail

REPORT OF CASES

CASE 1—A M R, a 32 year old Mexican Indian, entered the United States Naval Hospital, Treasure Island, San Francisco, on April 8, 1944, complaining of a painful right ankle and sores on his skin He was born in San Diego and prior to his enlistment in the Navy on Dec 13, 1943, had lived in San Diego county

On March 15, 1944, a nodule developed on his left forefinger and his right ankle became painful Several days later nodules appeared on the left cheek and on the right side of the forehead These nodules were at first small, reddish purple and smooth-surfaced but later became verrucous and elevated, with a purulent discharge

The physical examination revealed a small, thin man in no distress, with purulent verrucous nodules on the left forefinger, right side of the forehead and the left cheek (fig 1) There was widespread lymphadenopathy and a warm, tender, swollen right ankle The examination revealed no further abnormalities

1 Wernicke, R Ueber einen Protozoenbefund bei Mycosis fungoides(?), Centralbl f Bakt **12** 856, 1892

2 Posada, A Un nuevo caso de micosis fungoidea con psorospermias, An d Circ med argent **15** 585, 1892

3 Rixford, E A Case of Protozoic Dermatitis, Occidental M Times **8**.704, 1894 Rixford, E, and Gilchrist, T C Two Cases of Protozoan (Coccidioidal) Infection of the Skin and Other Organs, John Hopkins Hosp Rep **1** 209, 1896

4 Ophuls, W, and Moffitt, H C A New Mold (Formerly Described as a Protozoan Coccidioides Immitis Pyogenes), Philadelphia M J **5** 1471, 1900 Ophuls, W Further Observations on a Pathogenic Mold Formerly Described as a Protozoan, J Exper Med **6** 443 (Feb) 1905, Coccidioidal Granuloma, J A M A **45** 1291 (Oct 28) 1905

5 Dickson, E C Coccidioides Infection, Arch Int Med **59** 1920 (June) 1937, Valley Fever, California & West Med **47** 151 (Sept) 1937

The erythrocyte sedimentation rate was 30 mm per hour, and the white cell count was 7,750, with 6 per cent eosinophils The reaction in the coccidioidin skin test was positive Aspirated pus from fluctuant cervical lymph nodes contained the double-contoured highly refractive spores characteristic of coccidioidomycosis The early lesions became granulomatous, and new abscesses developed in the left knee, the left buttock, the left portion of the thorax and submental region The diagnosis was verified by culture, biopsy and guinea pig inoculation The lesions were treated by drainage and excision, and potassium iodide was given orally, with little or no improvement On May 5 the patient was given a course of penicillin extending over a seven day period and totalling 1,000,000 Oxford units, with no appreciable change Roentgenograms on August 23 revealed parenchymatous infiltration of the subclavian portion of the right lung and destruction of the bone of the left seventh rib, all previous roentgenograms had shown no abnormalities Treatment with coccidioidin vaccine, at first a stock supply and later an autogenous



Fig 1—*A*, noduloulcerative lesions of the face *B*, detail of lesion on left cheek, showing close resemblance to blastomycosis

vaccine, was started on July 18, 1944 and continued at two week intervals The patient continued to lose weight, became cachetic and debilitated and, on Jan 1, 1945, died

Abstract of Necropsy Protocol—Gross Findings Lungs The right pleural cavity contained 2,000 cc of pale yellow fluid flecked with fibrin The lower lobe of the right lung was atelectatic, while the apex revealed several small cavities from 1 to 5 mm in diameter, forming a honeycombed tissue surrounded by a solid white parenchyma These cavities were lined by a pale gray, granulating membrane No definite miliary or nodular granulomas were seen on gross inspection

The left pleural cavity was almost obliterated by fibrous adhesions The cut surface of the lung did not reveal any gross pathologic changes The tracheobronchial lymph nodes were enlarged up to 1 5 cm The cut section revealed extensive caseous and calcareocaseous destruction

Heart The pericardial sac was completely obliterated by firm, fibrous adhesions except for a linear pocket of thick pus along the left side of the heart Here the visceral and parietal layers were roughened by a thick, organizing, fibrinopurulent exudate which extended up over the base

Alimentary Tract The mesothelial surfaces of the mesentery and of the parietal wall were moderately studded with fine, white, glistening miliary lesions, of pinpoint

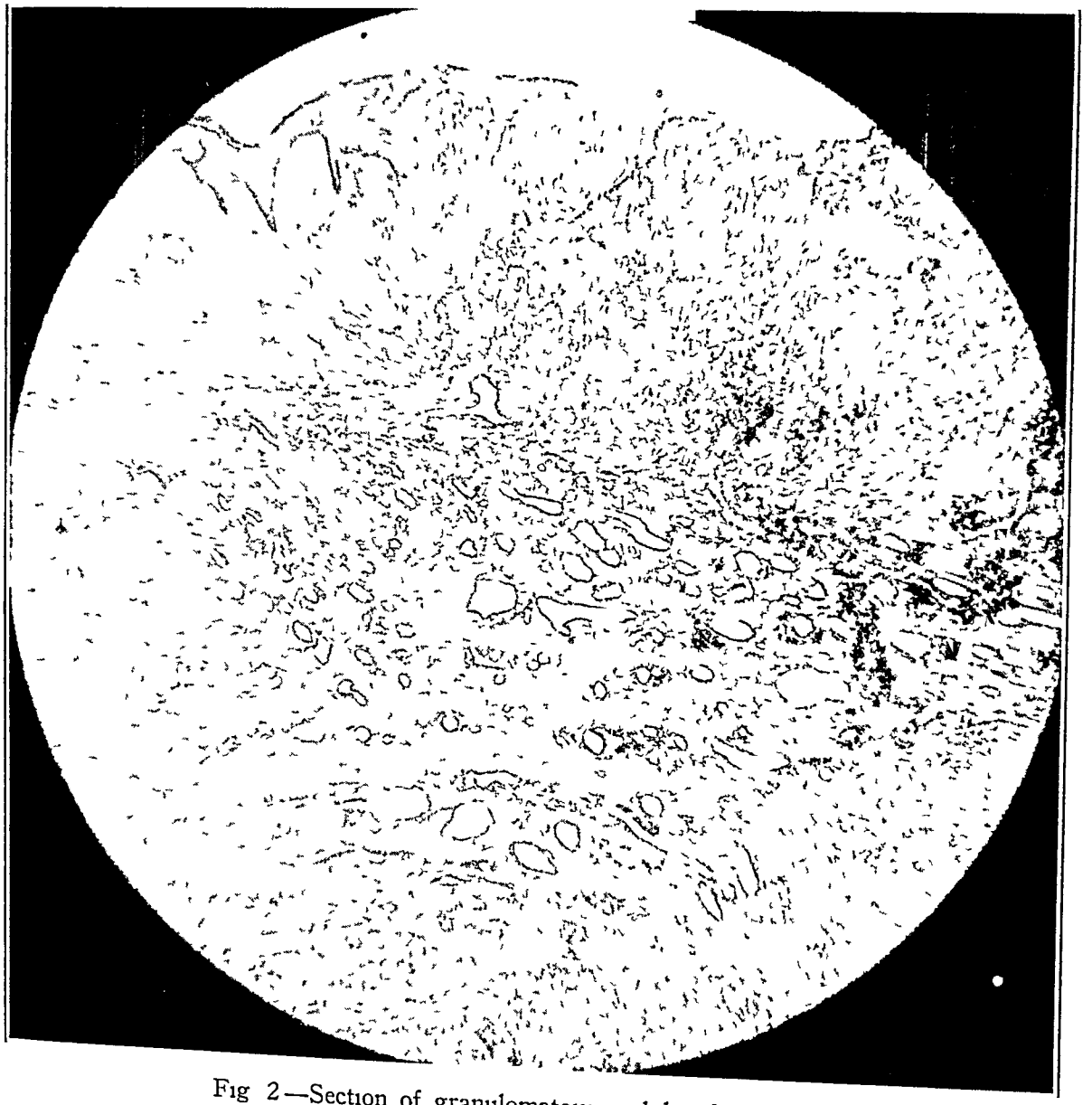


Fig 2—Section of granulomatous nodule of the face

to pinhead size Short fibrous tags were found along the mesenteric attachment and over the leaves of the mesentery

The esophagus was grossly normal except for a longitudinal lesion of 7 by 2 mm located on the anterior wall 7 5 cm below the rima glottidis The stomach had a pale pink and somewhat atrophic mucosa Three small, ulcerated outpouchings of the mucosa were located in the magenstrasse, 4 cm proximal to the pylorus These were about 3 to 4 mm in diameter, with smooth bases and borders The overlying serosa was thickened with fibrous tags The intestines

also contained similar small, shallow, ulcerated areas Their margins were formed by a delicate, pale, granular membrane, the overlying serosa was thickened by fibrous tags A solitary lesion was found in the duodenum, while about twenty-four such lesions were seen in the cecum and ascending colon Most of the lesions were 2 by 4 mm, with their long axes at right angles to the long axis of the bowel

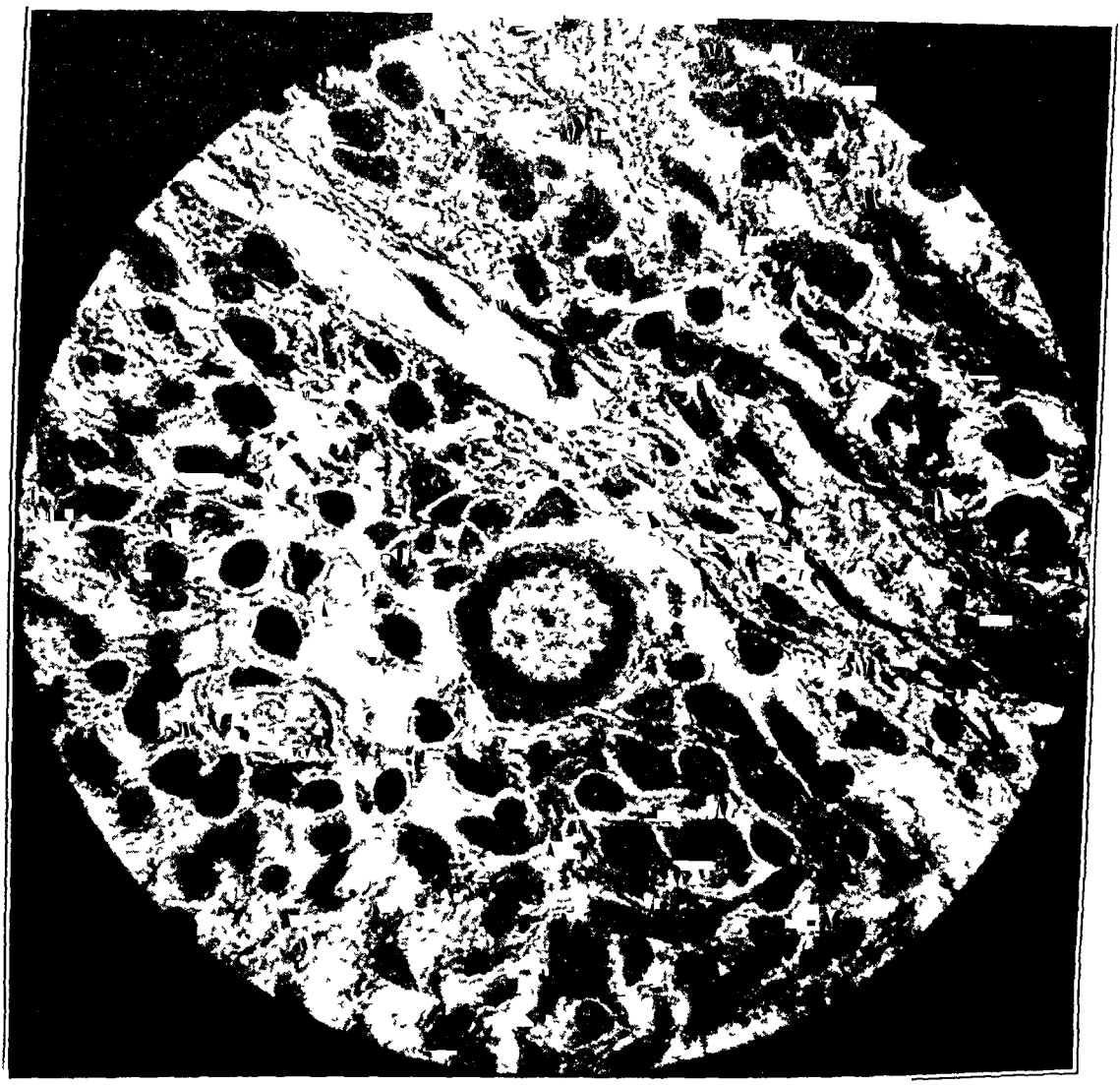


Fig 3—High power view, showing a characteristic mature endosporulating spherule

Osseous System The only significant bone lesion was a small area of osteomyelitis of the left seventh rib The cortex was irregularly thickened for a distance of 7 mm proximal to the medullary lesion on the pleural surface

Microscopic Observations (figs 2 and 3) In general the lesions were typical granulomas with numerous coccidioidal spherules The larger lesions showed tubercle formation, with central caseation The spherules were present free in the proliferating reactive border and within the Langhans giant cells The granulation tissue was composed of capillaries, proliferating endothelial cells and young collagen

connective tissue elements, a heavy infiltration of plasma cells and lymphocytes, tissue mast cells, mononuclear phagocytes with cell detritus and an occasional polymorphonuclear leukocyte Varying numbers and sizes of coccidioidal spores were scattered throughout this granulomatous tissue Many contained endospores, but in some instances they were devoid of these and appeared as empty cysts with double-contoured envelopes The cells of the tubercles were arranged in a

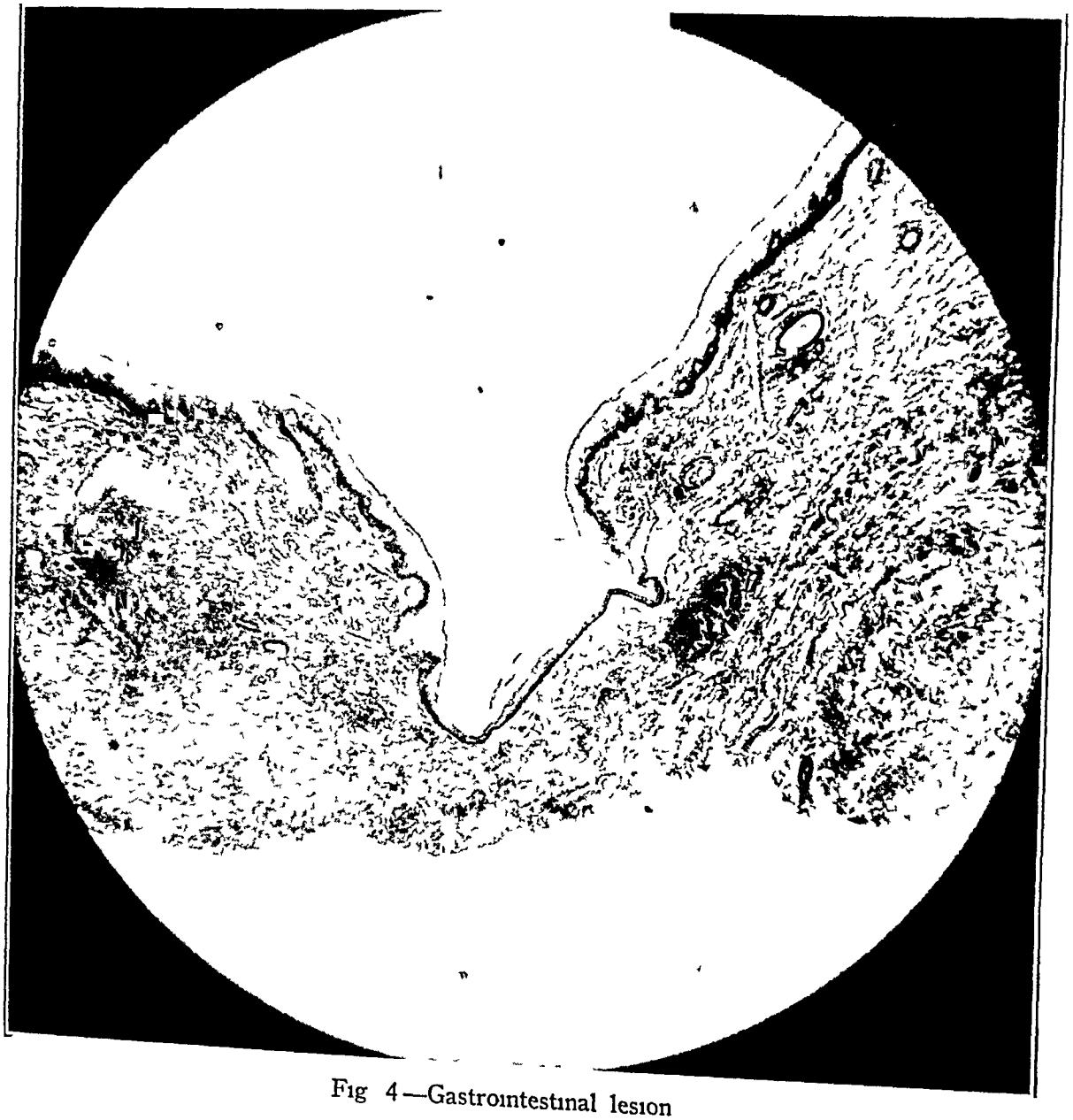


Fig 4—Gastrointestinal lesion

somewhat concentric, onionskin lamination The gastrointestinal lesions (fig 4) showed similar ulcerative granulomatous pathologic changes, involving the mucosa, submucosa and, to a lesser extent, the muscularis

Case 2—E A H, a 20 year old American Negro, was admitted to the surgical service of the United States Naval Hospital, San Diego, Calif, on Jan 26, 1946, complaining of pain in the right upper portion of the abdomen Prior to the completion of comprehensive laboratory examinations he constituted an interesting diagnostic problem, inasmuch as the differential diagnoses listed, among other

things, syphilitic hepatitis, subacute appendicitis, low grade hepatitis with multiple abscesses, parasitic infection of the intestine with perforation, trichinosis, secondary syphilis, nephrolithiasis, Loffler's syndrome, eosinophilic leukemia and pneumonitis

On January 24, epigastric pain, which lasted for about two hours, developed after meals On January 25, the patient had pain in the lower right anterior portion of the chest, but no dyspnea or infection of the upper respiratory tract, and afterward a persistent dull, aching pain appeared on the right side at the costal margin The following day, the patient first noticed two small papules, one on the midback and one over the epigastrium

The physical examination showed essentially normal conditions except for moderate tenderness in the right upper quadrant at the costal margin The abdomen was soft, and no masses or organs were palpable The chest appeared clear on auscultation and percussion Over the midepigastrium and midback there were two small, suppurating nodules



Fig 5 (case 2) —Showing lesions of lips and chin from which Coccidioides immitis was isolated

The erythrocyte sedimentation rate was 18 mm per hour, and the white cell count was 11,250, with 24 per cent eosinophils Subsequent blood counts all revealed an eosinophil count averaging about 14 per cent Repeated coccidioidin skin tests had negative reactions Reactions to the Kahn and Kline tests were initially positive, but to the Kolmer, Wassermann and repeated Kahn tests they were negative Biopsy of the nodule over the upper portion of the abdomen revealed numerous double-contoured, highly refractive spores characteristic of Coccidioides immitis Roentgenograms of the chest showed increased mottled markings of the central and lower central lung fields

The patient was put on a supportive regimen but continued to have a low grade fever He acquired new cutaneous lesions (fig 5) similar to the original two and rapidly began to fail as the pulmonary infection progressed C immitis was isolated from the purulent discharge of the ulcerating lesions He was given whole blood transfusions, 100 cc of protein hydrolysates (parenamine®) daily and 15 drops of

a saturated solution of potassium iodide three times daily On March 26, he was started on a course of penicillin, receiving 50,000 units every two hours for a total of 3,600,000 units His downward course progressed, and on April 2, just after completion of the course of penicillin, he began to exhibit signs and symptoms of cerebral involvement, which terminated in meningitis Spinal puncture revealed a grossly clear fluid which, on microscopic examination and later on culture, revealed C immitis On April 7, the patient died Postmortem examination revealed miliary coccidioidomycosis of the meninges, lungs, spleen and lymph nodes and a large granuloma of the sternum and the right second rib anteriorly There were many extradural abscesses The microscopic examination of all the tissues involved confirmed the gross findings, revealing typical lesions packed with C immitis

SYMPTOMATOLOGY AND CLINICAL COURSE

The infection assumes a wide variety of manifestations, ranging from the asymptomatic variety to the frequently fatal disseminated form, and can be best understood and discussed under the following classification proposed by Smith [6] Clinically it may be divided into three forms primary, intermediate and progressive

Primary Stage—In the majority of cases in the endemic areas, the onset of the initial infection may pass unrecognized or be interpreted as a mild infection of the respiratory tract This was probably the situation in 1 of our cases (case 2), in which the patient gave a history of an infection of the respiratory tract two months prior to his admission to the hospital On the other hand, the respiratory symptoms may be prostrating and more prolonged, accompanied by malaise, substernal pain in the chest, cough, night sweats and nasopharyngitis A small percentage of patients suffer a recurrence of fever in from three days to three weeks, associated with erythema nodosum or erythema multiforme, regarded as an expression of the allergic state While the disease in this stage is usually self limited, it must be remembered that a very small undetermined percentage may steadily progress to the disseminated form

Intermediate Stage—With a few exceptions the pathologic changes and symptoms in this stage are strikingly like those found in tuberculosis The findings may vary from the mildest to massive consolidation, cavity formation or scattered lesions resembling miliary tuberculosis, and the course may likewise vary in direct relation to the severity of the involvement Although cavity formation may occur without subjective symptoms, most patients complain of pleuritic pain and a productive cough Unlike the situation with tuberculosis, even patients with the most extensive pulmonary involvement recover, and the symptoms in relation to the amount of involvement are less severe than in tuberculosis Treatment is entirely symptomatic, with the elevation of the sedimentation rate the best guide for clinical management

Progressive or Disseminated Form—Fortunately the incidence of this form of the disease, which carries a very high mortality, is very low The incidence is definitely higher in the heavily pigmented races, of which both patients whose cases form the basis of this report were members The symptoms and the course vary with the organs involved, and the disease may terminate in death in a period of from a few weeks to a year In 1 of our cases the disease was more fulminating in type, terminating with meningitis in about two and one-half months, while in the other the patient lingered on for nine months Involvement of the bones, joints,

6 Smith, C E Coccidioidomycosis, M Clin North America **27** 790 (May) 1943

lungs, mediastinum and lymph glands is common, with the frequent development of verrucous and granulomatous nodules of the skin and subcutaneous cold abscesses The development of meningitis is evidence of wide dissemination and may occur with or without extensive visceral involvement The course of the meningitis is not unlike that of tuberculous meningitis, and, coincident with mental confusion in 1 of our cases, spherules of C immitis were demonstrated in the spinal fluid Gastrointestinal involvement is said not to occur because of digestion of the spherules, but Greaves [7] reported lesions in the small intestine and Ruddock [8] made the diagnosis by peritoneoscopy in a patient thought to have tuberculous peritonitis One of our patients (case 1) presented multiple lesions of the gastrointestinal tract, extending from the esophagus to the transverse colon They consisted of small, ulcerated outpouchings of the mucosa, 3 to 4 mm in diameter, with smooth bases and borders The margins of the ulcers were formed by a delicate, pale, granular membrane, the overlying serosa was thickened by fibrous tags The long axis of most of the lesions was at right angles to the long axis of the bowel

Treatment.—We are not concerned with the treatment of primary or intermediate coccidioidomycosis in this paper Suffice it to say that bed rest and symptomatic therapy will eventuate ultimately in clinical recovery, except in those cases with extensive cavitation, in which pneumothorax is required It is the progressive variety, of which the cases herewith presented are examples, that have so far been unaffected by a wide choice of remedies The drugs which have been of some value in other deep-seated mycoses, such as thymol, iodides, copper and antimony compounds and potassium tartrate, have uniformly failed to influence the course of the disease Penicillin offered nothing in our hands and has been reported by others [9] as ineffective Great hopes have been entertained for vaccines, but both the use of a stock and autogenous vaccine over a long period of time in increasing doses has been of no avail In order to rid the patient of large reservoirs of organisms which would otherwise be disseminated, all accessible granulomatous nodules were removed Roentgen therapy has been of no benefit, except to flatten exuberant granulomas The outlook in the progressive form of the disease must still be regarded as hopeless

EPIDEMIOLOGY

The epidemiology of coccidioidomycosis has become increasingly important because of the large numbers of men from all parts of the country brought into the endemic areas for training purposes during the past war and because of definite evidence of spread of the endemic areas For a long time after its first recognition, cases were reported only in those living in or near the great central valley of California It was not until 1920 that the first case east of the Mississippi was reported, and in the next decade there were accounts of sporadic cases in the Middle West and the eastern states A recent study by Smith [6] now reveals endemic areas occupying the great central valley of California and extending into southern California, all of Arizona, southern Nevada and southern Utah, probably parts of Idaho, all of New Mexico, western Texas and at least northern Mexico

7 Greaves, F C Coccidioidal Granuloma with Lesions in the Small Intestine, U S Nav M Bull **32** 201 (April) 1934

8 Ruddock, J C, and Hope, R B Coccidioidal Peritonitis Diagnosis by Peritoneoscopy, J A M A **113** 2054 (Dec 2) 1939

9 Michael, P , McLaughlin, R F, and Cenac, P L Coccidioidomycosis Report of Unsuccessful Treatment with Penicillin, U S Nav M Bull **43** 122 (July) 1944

One of our patients was born and remained in San Diego county until his entry in the Navy, while the other was born in North Carolina, his only possible contact with the organism coming while he was stationed in San Diego Lee's [10] experience with certain bodies of troops indicates a high percentage of infections when men are exposed to very dusty conditions in an endemic area The recent drought in California poses an additional hazard in the spread of the infection It has also been shown that animals in endemic areas harbor the infection, and the possibility of a rodent reservoir has been advanced Since the infection is carried in dust, the possibility of dissemination in vehicles and luggage of those traveling in and out of the endemic areas cannot be entirely discounted Although the danger on the present evidence is very slight, it is not yet definitely known whether or not the many thousands who were infected during their training period in an endemic area may have serious complications later in life

SUMMARY AND COMMENT

Much has been added to the knowledge and understanding of coccidioidomycosis in the past decade The endemic areas have been redefined and are known to extend over the southwestern United States and northern Mexico The patients in our cases undoubtedly contracted their infections in San Diego county, which had not been considered an endemic area They were both from dark-skinned races, in whom the progressive disseminated, frequently fatal form is most likely to develop Lesions of the gastrointestinal tract, which are said not to occur but have been recorded in the literature on one other occasion, were found widely distributed in 1 of our cases Although the infection in most instances is entirely benign and complete clinical recovery can be anticipated in even those who have pulmonary involvement with cavitation, possible serious complications may develop in later life in some of the many persons who were infected during their training period in an endemic area during the last war The similarity to and distinction from tuberculosis of this disease will become increasingly important to physicians everywhere, since these men have now returned to their homes throughout the United States Specific treatment is still lacking, and neither drugs nor vaccines have appreciably altered the course of the progressive disseminated form

3367 Fourth Avenue (3)

10 Lee, R V Coccidioidomycosis in the Western Flying Training Command, California & West Med **61** 133 (Sept) 1944

REACTIONS IN TATTOOS (CHRONIC DISCOID LUPUS ERYTHEMATOSUS)

JOHN F MADDEN, M D
ST PAUL

Reactions in tattoos generally fall into one of four groups The reactions in one group consist in the immediate response of the skin to the physical injury of tattooing This is rarely accompanied with or followed by secondary infection In

From the Department of Dermatology, Ancker Hospital, St Paul, Dr John F Madden, Director, and the Division of Dermatology and Syphilology, University of Minnesota Medical School, Dr H E Michelson, Director, Minneapolis

rare instances keloid,[1] melanoma,[2] severe pyogenic infection,[3] amputation,[3] gangrene [3] and even death [3] have been reported as direct consequences of tattooing

Allergic reactions to the material used in tattooing can occur immediately or at any time during the existence of the tattoo Allergic reactions to mercury, usually used in the red part of tattoos, have been most frequently noted [4] The allergic dermatitis may either be confined to the tattoo or be generalized The allergenic mercurial compound causing the dermatitis need not be the mercuric sulfide (cinnabar) in the tattoo, but it can be any form of mercury which is used on the skin or internally

Local or systemic disease can be injected into the skin at the time of the operation The manifestations of the injected disease may appear at once or later, the time depending on the particular characteristics of the disease Leprosy,[5] tuberculosis,[6] syphilis,[7] tetanus,[4f] erysipelas [8] and chancroid [8] are reported to have been contracted in this manner

1 Cipollaro, A C Keloid Following Removal of Tattoo Mark, Arch Dermat & Syph **36** 160 (July) 1937

2 Sharlit, H Melanoma Caused by Indelible Pencil, Arch Dermat & Syph **37** 301-306 (Feb) 1938

3 (*a*) Shie, M D A Study of Tattooing and Methods of Its Removal, J A M A **90** 94-99 (Jan 14) 1928 (*b*) Berchon, E Histoire medicale du tatouage, Paris, J B Bailliere & fils, 1869, Arch de med nav **11** 23, 107, 187, 294, 370 and 441, 1869

4 (*a*) Unna, P Quecksilberuberempfindlichkeit und Tatowierung, Arch f Dermat u Syph **160** 153-155, 1930 (*b*) Ballin, D B Cutaneous Hypersensitivity to Mercury from Tattooing Report of a Case, Arch Dermat & Syph **27** 292-294 (Feb) 1933 (*c*) Muller, O Ueber einen Fall von Hautgeschwulstbildungen auf dem Boden einer Tatowierung, Dermat Wchnschr **106** 6-8 (Jan 1) 1938 (*d*) Madden, J F Reactions in Tattoos, Arch Dermat & Syph **40** 256-262 (Aug) 1939 (*e*) Swinny, B Generalized Chronic Dermatitis Due to Tattoo Report of a Case, Ann Allergy **4** 295-296 (July-Aug) 1946 (*f*) Novy, F G, Jr Generalized Mercurial (Cinnabar) Reaction Following Tattooing, Arch Dermat & Syph **49** 172-173 (March) 1944 (*g*) Sulzberger, M B Tattoo Dermatitis (Sensitivity to Cinnabar?), ibid **36** 1265 (Dec) 1937 (*h*) Sulzberger, M B, Kanof, A, and Baer, R L Complications Following Tattooing Sensitization and Desensitization to Mercury, Report of a Case, U S Nav M Bull **43** 889-894 (Nov) 1944

5 (*a*) Abramson, P D Tattooing A Brief Review of Its History, Pathology and Methods of Removal, New Orleans M & S J **84** 191-195 (Sept) 1931 (*b*) Porritt, R J, and Olsen, R E Two Simultaneous Cases of Leprosy Developing in Tattoos, Am J Path **23** 805-817 (Sept) 1947

6 Abramson [5a] Gould, G M, and Pyle, W L Anomalies and Curiosities of Medicine, Philadelphia, W B Saunders, 1897, p 751 Collings, D W, and Murray, W Three Cases of Inoculation of Tuberculosis from Tattooing, Brit M J **1** 1200 (June 1) 1895

7 Novy [4f] Lacassagne, A Les tatouages Étude anthropologique et medico-legale, Paris, J-B Bailliere & fils, 1881, cited by Shie [3a] Maury, F F, and Dulles, C W Tattooing as Means of Communicating Syphilis An Investigation of Twenty-Two Cases Exposed to Inoculation with the Virus of Mucous Patches, in Fifteen of Which Syphilis Followed, Am J M Sc **75** 44-62 (Jan) 1878 Cheinisse, L Chancres syphilitiques multiples consecutifs au tatouage, Ann de dermat et syph **6** 1-5, 1895

8 Wilde, A G Vaccina Infected Tattoo Case Report, New Orleans M & S J **82** 385-386 (Dec) 1929



Fig 1—Lesions of chronic discoid lupus erythematosus on the face

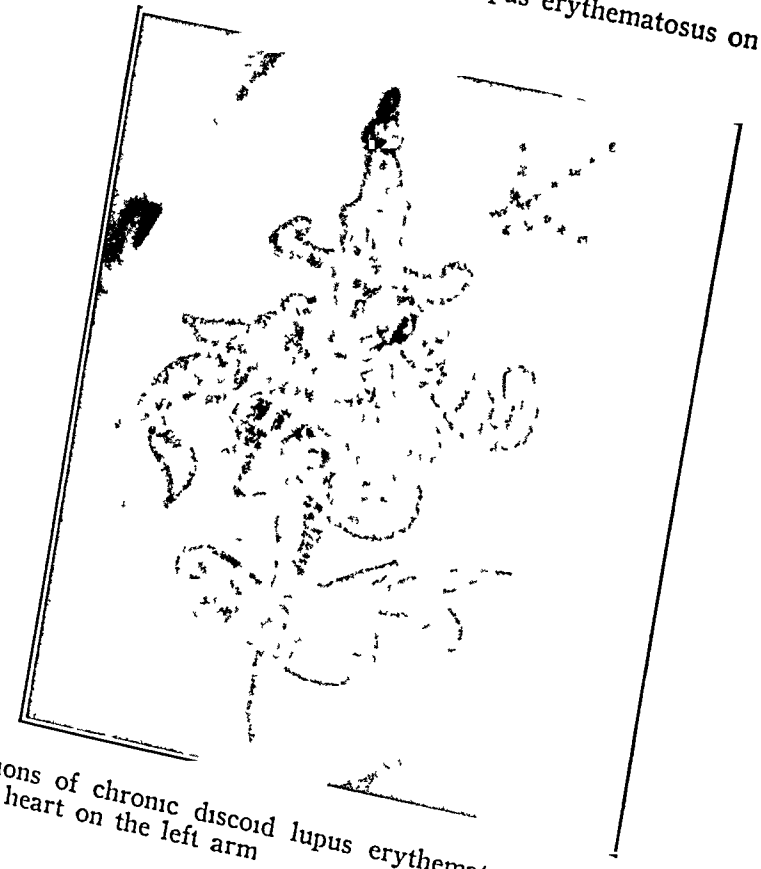


Fig 2—Lesions of chronic discoid lupus erythematosus in the upper half of the tattooed red heart on the left arm

The last group of reactions includes the appearance of local or systemic disease in tattoos after the tattoos have become a site of lowered resistance Brose [9] demonstrated that all portions of tattoos are more sensitive to blows, rubbing and external mechanical stimuli than is normal skin Belote [10] and others showed that tattoos alter the distribution of secondary syphilis The lesions were accentuated in and around tattoos except in the red (mercuric sulfide) portion, where the protective influence of the mercuric ion was greater than the effect of the foreign pigment in lowering the resistance of the area This paper records the first case known to me of chronic discoid lupus erythematosus occurring in a tattoo



Fig 3—Low power view of microscopic section taken from a lesion in the tattoo, showing histopathologic features in keeping with chronic discoid lupus erythematosus

REPORT OF A CASE

J C, aged 36, a white male truck driver, was tattooed on the lateral surface of the left arm in 1943 The tattoo healed after the initial reaction and showed no signs of irritation until November 1947 Then the red part of the tattoo began to itch and burn A dermatitis appeared in the red part of the tattoo in about a week. The patient stated that there was not any known cause for the symptoms

9 Brose Neue Tätowierungsphänomene, Dermat Wchnschr **84** 461-463 (April 2) 1927

10 Belote, G H Tattoo and Syphilis, Arch Dermat & Syph **18** 200-209 (Aug) 1928

or the eruption This development was accompanied by a similar dermatitis on the face, which also itched and burned In March 1948 the patient had scattered, pea-sized to dime-sized, dry, round, erythematous, pruritic papules covered with an adherent carpet-tack-like scale on the face and in the red part of the tattoo There were about fifteen lesions on the face and four in the tattoo Reactions in the Mantoux test and in serologic tests for syphilis were negative A roentgenogram of the chest and other laboratory studies showed normal conditions Biopsy specimens from lesions on the face and from the tattoo showed histopathologic features which were in keeping with the diagnosis of chronic discoid lupus erythematosus All lesions seemed to respond to bismuth subsalicylate in oil given intramuscularly On two separate occasions the eruption showed an acute flare-up when the face was exposed to sun and wind for about three hours All lesions flared, even though those in the tattoo were protected by a shirt and a heavy leather jacket

SUMMARY

A case of chronic discoid lupus erythematosus with characteristic lesions on the face and in the red portion of a tattoo on the left arm is reported Wind burn and sunburn caused the eruption to flare simultaneously on the face and arm even though the eruption on the arm was protected by a shirt and heavy leather jacket

1228 Lowry Building

IDENTICAL ALOPECIA AREATA IN IDENTICAL TWINS

OWEN S HENDREN, M D
BIRMINGHAM, MICH

In the past many dermatologic and nondermatologic diseases have been reported in twins To enumerate only a few, they are lichen planus,[1] von Recklinghausen's disease (neurofibromatosis),[2] rosacea,[3] summer prurigo,[4] ichthyosis hystrix,[5] peptic ulcers,[6] calcified mesenteric glands,[7] pilonidal cysts,[8] ephelides,[9]

From the Department of Dermatology and Syphilology, Wayne University College of Medicine, Detroit, and City of Detroit Receiving Hospital, Dr Loren W Shaffer, Director

1 Epstein, S Lichen Planus Confined in the Oral Cavity in Twins, Arch Dermat & Syph **45**.382 (Feb) 1942

2 Loftis, E L Recklinghausen's Disease in Identical Twins, Arch Dermat & Syph **42** 657 (Oct) 1940

3 Saunders, T S Rosacea in Twins, Arch Dermat & Syph **50** 269 (Oct) 1944

4 Parkhurst, H J Summer Prurigo of Hutchinson in Twins, Arch Dermat & Syph **14** 625 (Nov) 1926

5 Gross, P Ichthyosis Hystrix in a Twin, Arch Dermat & Syph **35** 520 (March) 1937

6 Riecker, H H Peptic Ulcer in Identical Twins, Ann Int Med **24**·878 (May) 1946

7 Hoffstaedt, E G W Identical Disease in Identical Twins, Brit M J **1** 516 (April) 1945

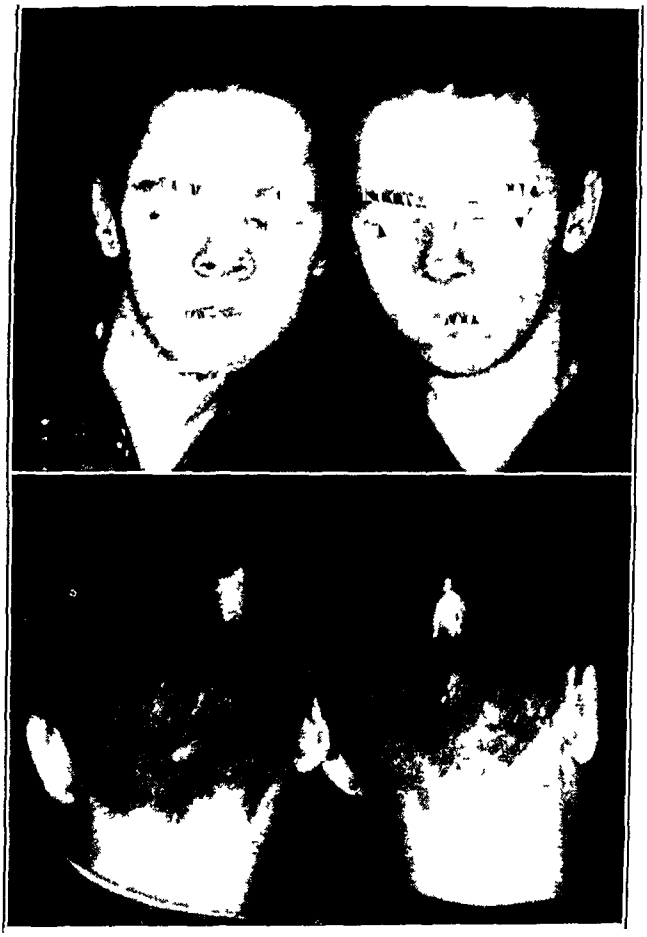
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lentigines,[9] and dermatitis herpetiformis.[9] There have also been reported several cases of allergy of similar type and onset.[10]

The following case of alopecia areata beginning at the same time on identical areas of the scalp in monozygotic twins aroused our interest.

REPORT OF A CASE

Robert L. and Raymond L., 11 years of age, presented themselves to the Dermatology Clinic, City of Detroit Receiving Hospital, on Oct. 31, 1947, with the complaint that each had a bald spot on his head. Their mother stated that



Showing similarity in appearance of the twins and small areas of alopecia areata in identical locations on the right side of the occiput.

these spots had been first seen by her on the same day in June 1947, that to the best of her knowledge both had appeared at the same time and that she was sure that they had not been present the previous week.

8. Fox, P. F.: Pilonidal Cysts and Sinuses in Identical Twins, J. A. M. A. **125**: 120 (May 13) 1944.

9. Melsom, R.: Dermatological Investigations on Twenty-Two Pairs of Identical Twins, Acta dermat.-venereol. **25**: 29 (June) 1944.

10. Criep, L. H.: Allergy in Identical Twins: Report of Seven Pairs of Twins, J. Allergy **13**: 591 (Sept.) 1942.

The family consisted of the mother, the father and 4 children No other member of the family had or ever had had a similar type of loss of hair Both patients had had measles and pertussis at 18 months of age Robert had had chickenpox when he was 6 years old, but Raymond had not There was no history of other previous illnesses

On examination the boys were strikingly similar in appearance, with the same shade of hair and with the same characteristics in regard to ears, teeth, nose and mouth In all zones of the iris of both patients there was the same type of pigmentation and distribution[11] Both boys exhibited a small area of typical alopecia areata in identical locations on the right side of the occiput approximately 2 by 0 75 cm Below each lesion there were three smaller areas of thinning of the hair but no complete loss in any place except those previously mentioned

Repeated examinations of the scalp under the Wood light revealed no fluorescence in the case of either boy Repeated cultures were negative for tinea capitis The hair appeared normal on direct microscopic examination Observations in blood counts (red cells, white cells and differential), as well as in urinalysis and serologic examinations, were all essentially normal

COMMENT

In a review of the literature for the past several years only 1 case of alopecia areata in twins was found,[12] and that case was somewhat different from the one here presented in that the lesions were not identical and did not appear simultaneously

Several theories have been advanced as to the cause of alopecia areata, but the exact etiology is unknown No single theory will account for all cases of the condition

In presenting this interesting and rather unusual case no attempt is being made to interpret the findings, and it is not our intention to try to prove or disprove any of the theories that have been advocated to date Rather, the case is presented purely as a dermatologic curiosity

1025 Pilgrim Road

11 Rife, D C Genetic Studies of Monozygotic Twins II Finger Patterns and Eye Color as Criteria of Monozygosity, J Hered **24** 407 (Oct) 1933

12 Turnacliffe, D D Alopecia Areata in Twins, Arch Dermat & Syph **24** 1122 (Dec) 1931

SUMMER PRURIGO

Report of a Case Controlled by Diphenhydramine (Benadryl®) Hydrochloride

HARRY W WOOLHANDLER, M D
PITTSBURGH

Summer prurigo is at best an incompletely understood entity While it is generally accepted that hypersensitivity to sunlight produces the eruption, the exact wavelength responsible has never been definitely established Experimental

From the Section of Dermatology, University of Pittsburgh School of Medicine

reproduction of this dermatosis has been accomplished with ultraviolet rays, ordinary sunlight, sunlight passed through window glass, yellow and red rays of longer wavelength only and even alpha and gamma rays [1] Attempts at desensitization have generally been unsuccessful, and, except for symptomatic treatment and avoidance of sunlight, no therapeutic measure of merit has been described Thus, the dramatic response to diphenhydramine hydrochloride (benadryl hydrochloride®) in a recently treated patient appears worthy of reporting

REPORT OF CASE

A 5 year old white girl was first seen by me on April 9, 1947, with an eruption of the cheeks and nose of four days' duration History obtained from the mother indicated that the patient had previously had a similar eruption lasting from June 1946 to October 1946, which initially had involved the face and the forearms At that time the patient had been seen by the family physician, who had prescribed daily exposures to sunshine After a few days of such exposures the eruption spread to the arms, legs and chest, with the lesions becoming moist and crusted for the first time There was no response to local applications, but in early October the eruption healed spontaneously The child's skin then remained entirely clear until April 5, 1947, when the eruption reappeared

Examination on April 9 revealed an eruption involving the cheeks and the nose and consisting of grayish red plaques, which on closer inspection were seen to be made up of closely set papules with adherent scales The lesions on the nose were entirely discrete, while those on the cheeks had coalesced into small plaques A diagnosis of summer prurigo was made, and on April 17 the patient was presented before the Pittsburgh Dermatologic Society, where this diagnosis was accepted by all except one member, who stated the belief that the disease was a dry staphylococcic infection

On April 9, the date of the first visit, the patient's mother was admonished to keep her out of direct sunlight, and a paste containing 3 per cent ichthammol (ichthyol®) was prescribed However, the mother permitted the child out in the sunlight as usual, and three days later the eruption had spread to the forehead and forearms, the original areas of involvement on the cheeks and nose having become more extensive A bland paste containing menthol, phenol, boric acid, zinc oxide, petrolatum and rose water ointment was substituted for the ichthammol paste and elixir benadryl hydrochloride® (a preparation containing 0 25 Gm diphenhydramine hydrochloride [benadryl hydrochloride®] in an elixir containing alcohol, glycerin and water, with sugar, flavoring oils and added color, in each 100 cc) 1 fluidrachm (3 7 cc) three times daily, was prescribed On April 17 the eruption showed no appreciable change, but on April 24 there was striking improvement, the face being almost entirely clear and the eruption on the forearms improved When the patient was next seen, on May 8, the skin of the face was entirely normal and the eruption of the forearms was barely discernible On June 7 no evidence of the original eruption could be seen, but a small area of involvement was found in the sternal region The child's mother admitted having permitted the girl out in the sun during a recent hot spell with no clothing except bathing trunks A promise was then exacted that the child would at no time be permitted outside with less clothing than a dress The sternal involvement

1 Becker, S W, and Obermayer, M E Modern Dermatology and Syphilology, ed 2, Philadelphia, J B Lippincott Company, 1947, p 291

healed in a few days, and no further relapses occurred during the entire summer Use of diphenhydramine hydrochloride was stopped on October 15, and there was no recurrence of the eruption up to Feb 15, 1948

COMMENT

An attempt was made during the management of this case to obtain consent to temporary discontinue use of the diphenhydramine hydrochloride (benadryl hydrochloride®), in order more definitely to establish the role of this drug in treatment of summer prurigo The mother's refusal prevented this or any other experiments from being carried out Nevertheless, I feel that the evidence, while presumptive, indicates that diphenhydramine hydrochloride was responsible for the control of this eruption At no time was any other medicament, except the bland paste mentioned, employed and the child was apparently exposed to direct sunlight regularly during the entire spring and summer That the diagnosis was probably accurate is attested to by the almost unanimous agreement of more than twenty dermatologists Further use of this drug in treatment of summer prurigo is definitely indicated, similar results would, of course, suggest that histamine plays a role in the causation of summer prurigo

8122 Jenkins Arcade (22)

SOLID CARBON DIOXIDE AS AN ANESTHETIC IN ELECTRODESICCATION OF CUTANEOUS BLEMISHES

ALEXANDER BREGMAN, M D
Associate Dermatologist, Englewood Hospital, Englewood, N J
EDGEWATER, N J

The electrodesiccation of cutaneous blemishes necessitates the use of local anesthesia because without it the procedure is too painful to be acceptable to patients Of the two methods of producing local anesthesia, namely, ethyl chloride freezing spray and infiltration with procaine or similar drugs, the local infiltration anesthesia is the more practicable Ethyl chloride spray is impracticable for two reasons It is inflammable, and thus unsafe for use in the presence of a spark, and the anesthetic effect wears off by the time the ethyl chloride has evaporated In using electrodesiccation for such lesions as pigmented moles or common warts in the region of the cartilaginous portion of the nose it is sometimes difficult for one to employ an anesthetic acting by local infiltration because of the close proximity of the underlying cartilage and lack of loose subcutaneous tissue which would allow infiltration with the anesthetic

Solid carbon dioxide used for its anesthetic effects works well in such situations It possesses the advantages of other types of compounds producing local anesthesia without exhibiting their drawbacks, and is less objectionable to the patient It is not inflammable, and it is of more lasting effect than is ethyl chloride spray, the latter characteristic being accounted for by the fact that ethyl chloride produces a temperature of about —31 F, whereas with solid carbon dioxide a temperature as low as — 110 F can be obtained

Although any type of machine for making solid carbon dioxide can be used satisfactorily for this purpose, I employ the Kidde dry ice® apparatus The whole

procedure of producing anesthesia by freezing does not take more than a couple of minutes I apply the solid carbon dioxide pencil for ten seconds with moderate pressure and then proceed with electrodesiccation

After having used this method on a few patients with lesions in the nasal region and having proved to my complete satisfaction its feasibility and practicability I began to employ it in producing anesthesia on other parts of the body whenever electrodesiccation was indicated—in treating small isolated lesions of various natures I submit this method in the expectation that others may try it to determine the possibilities of this simple and practical way of treating cutaneous blemishes

4 Dempsey Avenue

ALLERGY TO WAX CRAYONS

Report of a Case

MIRIAM LUTEN, M D
PORTLAND, ORE

In 1947, two reports of cases of poisoning by wax crayons appeared in the literature The first one, by Jones and Brieger,[1] described a child in whom symptoms of severe paranitraniline poisoning developed as a result of the patient's eating red and orange crayons In the second report, Clark [2] told of the case of a child who acquired methemoglobinemia from eating yellow and orange crayons Schwartz, Tulipan and Peck [3] stated that school teachers may acquire dermatitis of the terminal ends of the thumb and index fingers from the dye in colored crayons They found that among 81 workers in refineries manufacturing paraffin 19 had boils or acne on their arms and hands They found that oil and wax acne differs from acne vulgaris in that the eruption in oil and wax acne is oftener found on the body and legs than on the face, which situation they attributed to the plugging of the orifices of the hair and the sebaceous follicles, with formation of comedos which become secondarily infected They expressed the opinion that the percentage of wax warts, acne and pustules decreases in direct proportion to the purity of the paraffin handled and that workers handling the white, refined product are almost free from these conditions

REPORT OF CASE

S S D, a 7 year old girl, came to the office, complaining of sties which had been present almost continuously for four years For the previous two years she had had severe itching of the axillas and the buttocks, followed by many furuncles in these regions Treatment had consisted of stock and autogenous vaccines, stannoxyl® (a preparation containing 42 5 per cent metallic tin and 7 5 per cent tin oxide) and general hygienic measures, all without benefit There were no refractive errors

1 Jones, J A, and Brieger, H Poisoning Due to Ingestion of Wax Crayons Report of a Case, J Pediat **30** 422 (April) 1947

2 Clark, E R Poisoning Due to Ingestion of Wax Crayons Report of a Case, J A M A **135** 917 (Dec 6) 1947

3 Schwartz, L, Tulipan L, and Peck, S M Occupational Diseases of the Skin, ed 2, Philadelphia, Lea & Febiger, 1947, pp 240, 243 and 858

After the suggestion that this condition could be due to allergy, the mother could recall only one material that the child had used continuously during this time At 3 years of age, she had started playing with wax crayons every day Patch tests of wax crayons and fatty extracts of house dust and dog hair made on the skin around the axillas were indeterminate When crayons were taken away from the child, she was free from sties and boils for two and one half weeks, the longest period in the past four years She was given a crayon for two minutes Within one-half hour, her eyelids became red, and sties appeared on the lids by the next morning Perma® crayons, which the manufacturer stated are made by an entirely different process from that used in making the crayola,® produced sties after similar exposure During the succeeding months, infections on the lids followed the child's handling of pictures colored by other children and contact with candles Colored pencils, protected by wood covers, were tolerated for a short time only

Four trials were made with a piece of wax without dye, which was furnished by the manufacturer After one of these trials, a small sty appeared Smears made from the draining pustules contained diplococci The last trial with both uncolored and colored wax, one year later, caused only a generalized pruritus but no sties

The only local therapy used was tyrothrycin, which the mother believed shortened the duration of the lesions

Throughout the summer months, when the child was not in school or exposed to wax crayons, she remained free from cutaneous lesions, except for one episode in which a severe edema of the eyelids followed playing in weeds This edema disappeared almost at once when the child's face was washed Scratch tests at this time showed strong reactions to the pollen of English plantain

SUMMARY

A case is reported in which sties, furuncles and pruritus repeatedly followed exposure to wax crayons

919 Taylor Street Building (5)

Society Transactions

BRONX DERMATOLOGICAL SOCIETY

Wilbert Sachs, M D, *President*

Henry Silver, M D, *Secretary*

Feb 20, 1947

Lymphoblastoma, Tumors on the Forehead and Postauricular Subcutaneous Nodules Presented by DR MAX B KAMPF

Granuloma Annulare of the Legs with Keratotic Lesions Presented by DR LOUIS CHARGIN

Purpura Annularis Telangiectodes? Radiodermatitis? Hemostasis Dermatitis? Presented by DR PAUL GROSS

E B, a white woman aged 54, has had recurrent ulcerations on the feet for the past ten years In 1940 she was admitted to the Hospital for Joint Diseases because of multiple ulcers After the ulcers had healed many atrophic areas were found on the skin of both feet On the periphery of the atrophic patches were many bright red purpuric papules and telangiectases The diagnosis of purpura Majocchi was considered at the time, but the patient did not return for further treatment In October 1946 she was again hospitalized At that time large ulcers were present below the external and internal malleoli and on the dorsum of the right big toe Small ulcerations were also present on the dorsal and lateral surfaces of several toes of the left foot In addition, she had a seborrheic dermatitis of the nasolabial folds and eyebrows

The prothrombin time was increased to 30 seconds, and there was secondary anemia On October 16 the sedimentation rate was 70 mm in 45 minutes, on October 28, 45 mm and on, November 7, 15 mm The cholesterol content of the blood was 319 mg per hundred cubic centimeters, of which 30 per cent was free cholesterol and 70 per cent esterified cholesterol The thrombocyte count was normal The result of a tourniquet test for capillary fragility was positive The result of the Peck test with moccasin venom was positive on the forearm, thigh and the affected area

Treatment consisted of complete bed rest, applications of wet dressings with acriflavine and later of nitrofurazone ointment The patient was given ascorbic acid, 500 mg a day, vitamin B complex, folic acid, ferrous sulfate, and menadione The ulcers healed rapidly, and the patient was permitted to leave the bed for about an hour a day After two days of this regimen there developed purpuric macules and dark red puncta around the atrophic scars Some of these lesions changed into small necrotic ulcers the size of a pinhead

Since Dec 26, 1946, the patient has been receiving biweekly injections of moccasin snake venom No purpuric lesions have appeared recently, but there developed a small ulcer at the base of the left big toe

DISCUSSION

DR CHARLES WOLF I could not see any clinical manifestations of Majocchi's disease There is, however, a vasocirculatory disturbance present which produced sclerosis of the peripheral vessels I think that the pulsation in the dorsalis pedis is, if not entirely obliterated, at least decreased The atrophic changes are due to the sclerosis of the peripheral blood vessels

DR DAVID BLOOM Clinically the eruption resembles radiodermatitis No other diagnosis can be made from the appearance of the lesions tonight

DR MAX JESSNER I would be more inclined to regard this case as one of radiodermatitis, especially in view of the fact that ten roentgen ray treatments had been given to the area Moreover, the lesions suggest healed ulcers, perhaps with superimposed radiodermatitis The patient also presents a peculiar thickening of the skin of both knees, with yellowish discoloration, not unlike housewife's knee, which I do not remember ever having seen previously However, the usual keratosis in housewive's knee is missing here

DR LOUIS CHARGIN I agree with those who are of the opinion that this is not Majocchi's disease In Majocchi's disease the lesions are much smaller, situated higher up on the legs, usually there is some atrophy in the center, and the lesions are annular I cannot classify this process, but these scleroderma-like changes are not infrequently seen in elderly persons, particularly women

DR ERNST NATHAN The patient presents atrophic patches on the knees and on the legs, linear stripes along the tibias and scleroderma-like changes, all of which impressed me as acrodermatitis chronica atrophicans with scleroderma-like changes

DR WILBERT SACHS I do not consider radiodermatitis or scleroderma in this case Clinically, Majocchi's disease must be distinguished from Schamberg's disease and similar processes However, since Majocchi's presents a definite histologic picture, a biopsy would settle the diagnosis

DR PAUL GROSS As Dr Wolf stated, the cutaneous condition of this patient can be explained only by a vascular disturbance which leads to sclerosis of the peripheral blood vessels and atrophy of the skin The pathologic process accounts for the clinical manifestations consisting of telangiectasis, purpura, necrosis and atrophy This could be clearly followed by prolonged observation of the patient while she was in the hospital

The unusual feature of this case was the extensive ulceration which developed on the dorsa of the feet Because of this, it was difficult to consider the diagnosis of Majocchi's purpura unless there was something in the pathologic changes of the disease which could explain the atypical manifestations Actually necrosis has been described as part of the histologic picture of purpura annularis Apparently the severity of the vascular damage in this case produced sufficient necrosis to lead to ulceration Secondary infection may have been an added feature and has aggravated the formation of ulcers The improvement of the circulation by treatment with bed rest and antiseptic ointment brought about healing of the ulcers in a relatively short time If the ulcerations had been the result of a chronic radiodermatitis, the patient would have experienced severe pain, and healing would not have been prompt Prior to the patient's admission to the hospital, the case had been managed as a case of radiodermatitis without benefit

Dermatitis Herpetiformis Arsenical Keratoses and Pigmentation. Ulcer of the Leg Presented by DR ALEXANDER A FISHER

Senile Elastosis of the Neck (Pseudo Xanthoma Elasticum?) Presented by DR PAUL GROSS

A Case for Diagnosis (Necrobiosis Lipoidica? Tuberculoderm?) Presented by DR MORRIS LEIDER and (by invitation) CAPT CHARLES D BELL

Ragweed Dermatitis Presented by DR ALEXANDER A FISHER

P B, a man aged 64, was in good health and free from any cutaneous disease until September 1936, when he walked barefoot through some lots in Astoria, N Y A vesicular eruption appeared on the back of the feet and legs It was diagnosed as dermatitis due to poison ivy and persisted for five months

The eruption recurred in September 1937, affecting mildly the feet, legs, face, hands, forearms and scrotum It then became perennial, with exacerbations from September to May The most comfortable months were June and July

At present there are thickened lichenified lesions on the face and forearms On the face the eruption is sharply limited to the upper part of the forehead

Patch tests with the following oleoresins gave positive reactions short ragweed, cocklebur, sheep sorrel, Kentucky blue grass, red top, short poison ivy, orchard grass and timothy Patch tests with protein extracts of trees, grasses and weeds showed a positive reaction only to oak Results of scratch tests with these protein extracts were negative The result of a patch test with a 5 per cent glycerine solution of ragweed oil (Hollister-Steer) was negative The patient has received oral treatment with oleoresins according to the Shelmire method

DISCUSSION

DR RUDOLF L BAER The patient had a positive reaction to the so-called "protein" fraction of the oak pollen I do not know whether there is any evidence that the oak protein has been of clinical significance Among the extracts available for testing, the "protein" fraction of oak pollen was included Unfortunately, no acetone extract of oak was available, so that it is impossible to state whether this patient is also sensitive to the oil fraction

It is probable that the fractions contained in various extracts differ considerably A patient suffering from a similar eruption at the New York Skin and Cancer Unit was tested with the following ragweed extracts (*a*) the oleoresin, (*b*) the so-called "protein" fraction in a glycerinated extract and (*c*) the so-called "protein" fraction in a powdered extract This patient reacted to the oleoresin fraction and to the powdered "protein" extract but not to the glycerinated extract, which is supposed to contain the same fraction as the powdered extract This indicates that there is a great difference between preparations which, it is assumed, contain the same fraction

DR CHARLES WOLF The history indicates that this patient was exposed to various flowers and pollens a long time ago, but not recently Still he exhibits a fairly pronounced eruption on the face and forearms, although he has not been in contact with these suspected allergens How can one explain the fact that the dermatitis still persists? Is it possible that this patient's sensitivity is polyvalent and reacts to many agents? What is the therapeutic approach to this problem?

DR MARION B SULZBERGER In the preparation of plant extracts with the usual variety of solvents, one extracts a great number of different substances in each of the fractions Dr Coca and I have demonstrated that in the case of allergic contact dermatitis to ragweed and to certain other plants it was a fat-solvent soluble fraction which contained the usual allergen This might be misinterpreted The fact is that in most common forms of allergic eczematous contact dermatitis, water-soluble materials, including many dyes, metallic salts and local anesthetics, are responsible

DR ALEXANDER A FISHER This case is puzzling Some are of the opinion that the oil remains in wearing apparel for many months There is also, as Dr Wolf suggests, a possibility that this patient became allergic to pyrethrum, which is related chemically, and that is what causes the eruption to become perennial As Dr Sulzberger pointed out, the aqueous fraction is frequently responsible for the dermatitis The Mitchells have reported a case of the disease due to aqueous fraction of timothy which they were able to cure by injections of the ordinary extract used for hay fever

Angioma Resembling Idiopathic Multiple Hemorrhagic Sarcoma Presented by DR HARRY B FEILER

Wilbert Sachs, M D, *President*

Henry Silver, M D, *Secretary*

March 20, 1947

Erythroplasia (Cured by Application of a Mixture of Neoarsphenamine, Glycerin and Water) Presented by DR WILBERT SACHS and DR PERRY M SACHS

Erythroplasia of Queyrat (No Biopsy) Presented by DR CHARLES PINES

Poikiloderma Vasculare Atrophicans (Jacobi) Presented by DR FRANCES PASCHER

Pityriasis Rubra Pilaris Presented by DR DAVID BLOOM

F C, a woman aged 57, registered at the Skin and Cancer Unit of the New York Post-Graduate Hospital on Feb 14, 1947, complaining of an eruption of five weeks' duration The past and family histories were irrelevant

The patient presents on the face erythematous scaly plaques which toward the neck are associated with spinulous follicular keratotic plugs On the anterior and posterior aspects of the trunk there are irregularly shaped, erythematous scaly patches and groups of keratotic follicular yellowish or skin-colored papules or plugs the size of a pinpoint or pinhead On the extensor surfaces of the forearms and hands, lateral aspects of the arms and thighs, there is a similar eruption The scalp shows diffuse scaling On the forehead and around the eyes there are numerous small fibromatous lesions and skin tags The palms and soles show considerable brownish-yellowish hyperkeratosis

The patient has no subjective complaints and seems to be otherwise in good health

Results of laboratory examinations, including urinalysis, a Wassermann test of the blood and a determination of the vitamin A content of the blood, were normal The blood cell and differential count showed an abnormal low white cell count of 3,500 and relative lymphocytosis (56 per cent lymphocytes) The report of the histologic examination of an erythematous lesion taken from the abdomen was possible early exudative lichenoid discoid dermatosis

DISCUSSION

DR WILBERT SACHS Microscopically there is no evidence of this disease The picture is that of exudative discoid and lichenoid dermatosis Recently Dr Perry Sachs and I reported 3 cases occurring in female patients (*J Invest Dermat* 8 215, 1947)

DR PAUL GROSS I agree with Dr Bloom that this is a case of pityriasis rubra pilaris The patient has leukopenia, it would also be of interest to make a complete hemogram I recommend treatment with crude liver extract and folic acid

DR DAVID BLOOM I presented this case because it is clinically typical, and yet the results of the histologic examination did not confirm the diagnosis It should be noted that when the biopsy specimen is taken from an erythematous plaque in which the keratotic papules have disappeared the pathologist is unable to make a diagnosis of pityriasis rubra pilaris I wish also to mention that a majority of the patients with pityriasis rubra pilaris that I have observed were all in the fifth decade and not young persons as mentioned in dermatologic textbooks

DR PAUL GROSS O'Leary makes a distinction between pityriasis rubra pilaris and pityriasis-rubra-like eruptions I think that this division is justified by the clinical picture, course and response to therapy I cannot agree with Dr Bloom concerning the age groups involved I have seen several children with extensive eruptions, usually with a sudden onset, showing the clinical features of pityriasis rubra pilaris These patients have shown a dramatic response to a combination of vitamin B complex and vitamin A

Early Mycosis Fungoides, Psoriasiform Lesions Presented by DR ADOLPH ROSTENBERG and DR WILLIAM M SISKIND

Idiopathic Onycholysis, Improved with Thyroid and Vitamin A Therapy Presented by DR ALEXANDER A FISHER

V C, aged 16, first noticed about three years previously that the nails became soft and separated from the nail bed

When first seen, on Dec 17, 1945, all finger nails were involved (kodachrome® slide presentation) He had been under the care of another dermatologist for one and one-half years and had received roentgen ray treatment, ultraviolet rays and various ointments without apparent effect

Results of the physical examination were normal except for a pulse rate of 82 A medical consultant stated that at this age basal metabolism readings are not reliable, and the basal metabolic rate was therefore not established The patient was given thyroid, ¼ grain (16 mg) three times a day

When he returned in a week the pulse rate was 92, and he complained of nervousness The dose of thyroid was then reduced to ¼ grain twice daily, and he was given, in addition, vitamin A, 100,000 units daily, to augment the

thyroid therapy For four months there was no change in the nails By June 1946 there was definite improvement, which has been continuous At present all the nails have practically returned to normal

DISCUSSION

DR PAUL GROSS There is a definite relationship between the thyroid and the vitamin A metabolism In cases of hypothyroidism there is frequently a vitamin A deficiency The excellent therapeutic result obtained by Dr Fisher is noteworthy

DR EMANUEL MUSKATBLIT It seems to me that onycholysis is not always of the same origin Some of these cases have an occupational background In others a separation of the nail from its bed results when the patients constantly soak their hands in water In such cases removal of the cause results in a cure

DR HENRY SILVER I consider the point raised by Dr Muskatblit pertinent The role of continuous use of soap and water should not be underestimated, particularly in patients with systemic disturbances The condition in this case, with the manifest thyroid disturbance, may well fall in this group (Silver, H, and Chiego, B Brittleness of Nails, *J Invest Dermat* **3** 5, 1940)

DR ALEXANDER A FISHER In spite of this boy's washing his hands many times a day, he is improving with vitamin A and thyroid therapy Moreover, it is strong alkali which causes onycholysis, and he denies the use of strong soaps

Circumscribed Scleroderma (Treated with Promin®). Presented by DR HARRY B FEILER.

L S, a woman aged 74, has been complaining of pain, burning sensation and tightness of the skin of the chest In May 1946, she noticed a patch about 3 by 1½ inches (8 by 4 cm) in diameter, located on the right side of the chest, which was hard, white and glistening and was surrounded by a violaceous border At present the lesion is still of the same size The blanched area is somewhat softer and has the remnant of the violaceous border Recently a few linear lesions appeared above the involved area

The patient has been given polyvitamins by mouth, and, with this regimen, there was a disappearance of the leathery consistency in the lesion, but otherwise there was no change She has received intramuscular injections of 50,000 units of vitamin A every second day for three weeks without any noticeable improvement

For the past week promin® (sodium p,p'-diaminodiphenylsulfone-N,N'-didextrose sulfonate) jelly has been applied There developed dermatitis at the site of the lesion accompanied with pain and burning sensation Treatment with promin® was discontinued

DISCUSSION

DR DAVID BLOOM Morphea may disappear without treatment Unless the effect is rapid, one cannot prove that promin® is therapeutically useful in morphea

DR ALEXANDER FISHER If no improvement takes place with promin® I would suggest bismuth subsalicylate Dr John A Stokes first mentioned this type of therapy Several patients at the Skin and Cancer Clinic have improved with treatment with bismuth preparations

DR. CHARLES R REIN Dr Carol Wright and Dr Elmer Gross have had excellent results in the treatment of scleroderma with a bismuth preparation (bistrimate®) given orally

Wilbert Sachs, M D, *President*
Henry Silver, M D, *Secretary*
April 17, 1947

Superficial Epitheliomas, Treated with Podophyllin Presented by DR JOHN GARB

M B, a man aged 73, was first seen on July 17, 1946, presenting three cutaneous lesions He had pneumonia in 1916 He has otherwise been in good health

The largest of the three lesions is located on the left lower border of the anterior part of the chest and epigastrium It is roughly round, 3 inches in diameter (7 5 cm) and dry, with a slightly raised border In that circle are several raised, crusted, irregular, dark red to purplish lesions, which are rough to the touch Most of the lesions have cleared with topical remedies and with exposures to ultraviolet rays, leaving a slightly darker but normal-appearing skin This lesion has been present for the past four years On the inner third of the right clavicle there is a similar patch 1 cm in diameter and an oval patch with axes of 7 and 5 cm on the left side of the back There is a scar in the midportion of the back as a result of an operation performed in 1945 for a carbuncle

The routine laboratory tests showed no abnormalities

Sections were taken from specimens of lesions on the front and back of the chest and examined histologically by Dr Charles F Sims The former showed a somewhat irregular epidermis At one point, extending down into the corium on the under surface of the basal margin, was a small mass composed of basal cells The vessels of the upper part of the corium were moderately dilated and surrounded by mild interstitial edema and a nonspecific cellular reaction From the histologic examination the diagnosis was superficial basal cell epithelioma

Microscopic examination of the specimen taken from the lesion of the back showed features of superficial dermatitis

An ointment containing 5 per cent podophyllin prepared with 8 Gm of castor oil and aquaphor® (an oxycholesterol-petrolatum ointment base), enough to make 2 ounces (57 Gm), was applied on January 30 to the lesions of the chest On February 1, the lesions became ulcerated and a soothing ointment was applied On February 18, the rim of the lesion on the frontal part of the chest was still visible but not raised On February 25, the upper part of the patch on the back was still elevated On March 4, an ointment containing 10 per cent, and on March 11 and 13, 20 per cent of podophyllin was applied to a few spots on the frontal part of the chest On March 31, the 10 per cent ointment was applied to a few spots on both lesions On April 10, the lesion on the back appeared healed except for slight roughness The lesion on the front part of the chest was flattened to the level of the surrounding skin surface The border was still visible because of the brownish pigmentation A section was taken from the pigmented border close to the scar of the original section which showed basal cell epithelioma The histologic examination by Dr A M Sala showed atrophy of the epidermis and moderate round cell infiltration of the corium which appeared somewhat edematous There was no histologic evidence of neoplastic tissue

DISCUSSION

DR MARION B SULZBERGER The lesions give the impression of a superficial epithelioma either entirely healed or in the process of healing Whether a recurrence will take place one cannot foretell Several points need be considered

Certain superficial epitheliomas respond quickly to many forms of therapy Mild caustics and other superficial destructive measures may cure most superficial and small basal cell epitheliomas In evaluating any new therapy, one should keep in mind the ease with which nonspecific measures can remove these so-called carcinomas

Podophyllin is a peculiar substance which has some influence on mitosis As Maurice Sullivan, Lester S King and others have pointed out (in Wise, F, and Sulzberger, M B Yearbook of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc, 1946, p 510), podophyllin, like colchicine, somehow affects the nuclear metabolism and one sees many cases of arrested mitosis, all in the same phase—the metaphase, I believe It is, therefore, possible that podophyllin or podophyllotoxin may have some specific effect on the multiplying cells of the carcinoma and that the results achieved may be more than a mere nonspecific destructive action The action of podophyllin is well worth studying in relation to epithelial growth and deserves a good deal of further careful experimentation

Dr Frank E Cross New methods of therapy that are simple and promising should be encouraged, on condition that they are as good as or better than the older ones Dr Sulzberger just stated that podophyllin seems to have a basic action in that it interferes with mitosis On the other hand, I take exception to his statement of the "simplicity of ordinary epitheliomas" It is true that a treatment of some basal cell epitheliomas is simple, in others, however, radical measures must be resorted to

Dr Wilbert Sachs A biopsy specimen taken from the "healed" area will determine whether any carcinomatous tissue still remains

Dr John Garb The patient had the lesion on the left lower border of the chest and the epigastrium for forty years A biopsy specimen taken from the pigmented margin adjacent to the original histologic section did not show any epitheliomatous change The patient was not presented tonight as cured He will be kept under observation

Dermatitis Due to Gold, Successfully Treated with BAL (2,3-Dimercaptopropanol) on Two Occasions Presented by Dr Marion B Sulzberger

DISCUSSION

Dr Adolph Rostenberg I used BAL in a case of a widespread dermatitis of unknown cause, and the result was excellent It required several weeks of treatment, but after one injection there developed a severe nitritoid reaction, such as is observed after administration of arsphenamine preparations I have never observed it since and wonder whether this reaction occurs commonly

Dr David Bloom Before administration of BAL the cardiovascular status of the patient should be determined A few weeks ago I observed a patient who received BAL for suspected intoxication due to bismuth This patient, who received an excessive dose of BAL, had a severe reaction manifested by a sensation of burning and constriction about the mouth, face and chest The patient appeared rather ill It was later discovered that this patient had myocardial damage

Dr Marion B Sulzberger This patient was presented to demonstrate therapeutically the effectiveness of BAL in dermatitis due to gold One interesting feature in this case is that the BAL therapy has been effective twice The eruption got worse when BAL therapy was discontinued and then rapidly improved with readministration The therapy was stopped for the reasons given by Dr

Bloom There was slight albuminuria and a systolic blood pressure of 180 mm For that reason Dr Jessner thought it wise to discontinue the BAL therapy when the patient had improved

BAL is a powerful drug and one must be careful, particularly in patients with hypertension One good feature is that BAL is rapidly excreted, and the side effects are usually evanescent It is usual for the blood pressure to rise, however, this is variable, and I have often seen the blood pressure fall after BAL injections Because of the effect of BAL on blood pressure Dr Harry Gold of Cornell University expressed the belief that BAL might be valuable in treatment of certain peripheral vascular diseases It is effective also in allergic dermatitis and other conditions produced by certain metals and is often life saving in cases of allergic dermatitis due to mercury and arsenicals I would estimate that only about half of my patients with arsenical dermatitis have shown rapid and unequivocal improvement Theoretically one should expect a favorable response from BAL applied locally However, BAL is a strong cutaneous allergen, hence as a rule one cannot use it as an external application

A Case for Diagnosis (Sarcoid?) Presented by DR MAX BERKOVSKY

A Puerto Rican, aged 60, was admitted to the dermatologic service of the Metropolitan Hospital on March 20, 1947 There appeared on the left thigh a flat, sharply defined lesion the size of a dime, associated with some itching but no pain Similar spots appeared on all four extremities during the next three months The family history revealed that forty years ago the patient was intimately exposed to active tuberculosis in a relative who subsequently died of the disease The patient stated that to his knowledge he never had gonorrhea or syphilis

In 1932 he had an abscess of the left thigh which was opened and drained In 1939 cardiac decompensation developed Digitalis therapy was instituted, and the patient was discharged much improved In the fall of 1946 he was treated at the Harlem Hospital for a cough, and in three months he was discharged as cured He has lost 15 pounds (7 Kg) in the last ten years The only drug that he takes is feen-a-mint® (a laxative containing phenolphthalein) about twice a month

Physical examination reveals a well developed but poorly nourished man The systolic blood pressure is 180 and the diastolic pressure 90 The skin shows many nummular dark brown sharply demarcated flat-topped nodules with some infiltration They are symmetric and not tender and at present involve all four extremities and to some extent the chest and back

The Wassermann, Kahn and Kline reactions of the blood were negative Urinalysis showed no abnormalities Examination of the blood showed 82 per cent hemoglobin, 3,750,000 red blood cells and 12,200 white blood cells, with 40 per cent polymorphonuclear cells, 32 per cent lymphocytes, 15 per cent eosinophils, 11 per cent monocytes and 2 per cent basophils

Roentgenograms of the chest revealed a round shadow the size of a baseball in the region of the left hilus and extending into the anterior mediastinum This was diagnosed as a dermoid cyst, a teratoma or a benign cystic mass Roentgenograms of the hands showed no abnormalities The reaction to the tuberculin test was negative Histologic examination of specimens taken from the left thigh and left arm showed edema and hyalinosis of the papillae with perivascular infiltration of small round cells There was no evidence of tuberculosis The diagnosis from histologic study was chronic dermatitis of unknown cause

Results of examination of the bone marrow obtained by puncture of the sternum were not diagnostic It showed a decreased cellularity (hypoplasia) with good myeloid distribution, moderate eosinophilia and normal megakaryocytes

During the three weeks' stay at the hospital the patient's condition has remained unchanged A consultation was held with the thoracic surgeon concerning the tumor in the left anterior mediastinum A tentative diagnosis of teratoma or echinococcus cyst was made and exploration advised

DISCUSSION

DR DAVID BLOOM This eruption resembles sarcoid as seen in white persons It would be of interest to study the effect of calciferol in this case

DR LOUIS CHARGIN What is the pathologic report in this case?

DR FRANK E CROSS Clinically the lesion in this case is sarcoid, in spite of the lack of confirmation on histologic study It is possible that the biopsy specimens were taken from nonspecific sites Another biopsy specimen should be taken from a characteristic lesion and examined by a dermatopathologist

DR MAX BERKOVSKY Three biopsy specimens were taken and examined by the general pathologist at the Metropolitan Hospital and Dr Hyman at the New York Post-Graduate Hospital At no time could one justify the diagnosis of sarcoid on histologic study The reaction to the tuberculin test (1 10,000) was negatives Roentgenograms of the bones showed no abnormalities Roentgenographic examination of the chest revealed a mass which the surgeon said was a dermoid cyst in the anteriomediastinal space

DR. PAUL GROSS What has been done to rule out tuberculosis?

DR MAX BERKOVSKY No tuberculoid tissue was found on histologic examination There is nothing to warrant a diagnosis of leprosy

NOTE—The mediastinal tumor was removed by operation, and the histologic examination revealed a thymoma Subsequent histologic studies of cutaneous nodules by Dr W Sachs showed characteristic observations of lymphatic leukemia

Reticulum Cell Sarcoma Presented by DR DAVID B BALLIN

M M, a man aged 44, was previously presented before the New York Dermatological Society on Feb 25, 1947, by Dr Fred Wise, with the following note Additional data, such as results of the pathologic study of the left epitrochlear lymph node excised, roentgenogram of the chest, general medical examination, sternal puncture and electroencephalogram will be reported later

The patient is presented to show the rapid regression after 1 skin unit of roentgen rays (450 r) and to report the results of laboratory studies A hemogram taken on February 20 showed 5,160,000 erythrocytes, 1 8 per cent hemoglobin and a color index of 1 05 There were no eosinophils The results of sternal puncture and examination of the lymph node excised from the left epitrochlear region were reported as normal

Examination on April 16 revealed considerable regression in the satellite lesions about five weeks after the biopsy specimen was taken, but there was no diminution in the size of the main growth On April 3 1 skin unit of roentgen rays filtered through 1 mm of aluminum (450 r) was applied to the main lesion and about

2 inches (5 cm) beyond When the patient was seen on April 15 the growth was entirely flattened out, so that it was only slightly elevated above the surrounding skin

Lichen Planus, Lichen Nitidus Presented by DR JOSEPH L MORSE

R S, a boy aged 7 years, was first seen at the Hospital for Joint Diseases with a generalized fine branny desquamation The mother stated that about three weeks previously the child had a generalized rash accompanied with fever A diagnosis of postscarlatinal exfoliation was made Urinalysis at that time showed a faint trace of albumin

The patient returned to the clinic in July 1946 presenting a number of discrete, somewhat lichenified patches around both ankles Under treatment with bland ointments the condition improved over a period of two months

In March 1947 the patient again visited the clinic At this time he had an eruption on the ankles, elbows, knees and dorsa of the fingers (terminal phalanges) On the ankles there were areas made up of violaceous shiny papules, on the elbows and knees there were many small flesh-colored papules, some in linear arrangement along scratch marks (Koebner phenomenon) There were no lesions on the trunk or genitals A diagnosis of lichen planus and possible lichen nitidus was made

A specimen taken from a lesion of the right elbow showed the epidermis to be covered by a thin keratin layer The basal cells were heavily pigmented At one point, just beneath the epidermis, there was a localized collection of inflammatory cells, including mononuclear cells and polymorphonuclear leukocytes The epidermis overlying this nodule of inflammatory cells appeared somewhat compressed and thinned out The histologic picture was consistent with a diagnosis of lichen nitidus A roentgenogram of the chest showed no abnormalities Results of quantitative tuberculin (human and bovine) tests in dilution of 1 10,000 and 1 100,000 were negative Kahn and Kline reactions of the blood were negative The urine was normal

DISCUSSION

DR MAX JESSNER The question of the occurrence of lichen planus and lichen nitidus simultaneously is an old one The patient shows definite lichen planus on the ankles, the lesions on the arms resemble lichen nitidus At the outset the lesions look almost alike There have been cases reported in which the two types have been found together One should, however, have histologic evidence in order to corroborate both diagnoses I think that the picture in this case fits in with the lichen planus type, especially in view of the lesions on the ankle

DR PAUL GROSS The case is of interest because of the rare association of lichen planus and lichen nitidus The tissue was somewhat damaged in the preparation for histologic examination, and, therefore, a definite diagnosis of lichen nitidus could not be made The typical tubercle-like structure was lacking, but it may be that even in lichen nitidus a nonspecific granuloma is present in the early stage of the lesion

DR WILBERT SACHS Conclusions cannot be drawn from this slide I agree with the diagnoses of lichen planus and lichen nitidus I have seen 2 similar cases

DR JOSEPH L MORSE As Dr Gross pointed out, this case was presented because of the rare association of the two diseases The lesions around the ankles were certainly characteristic of lichen planus An effort will be made to obtain biopsy specimens from both types of lesions

Tinea Glabrosa, Dermatophytosis, Onychomycosis, Pityriasis Versicolor, Erythrasma and Tinea Versicolor Appearing in the Same Patient Presented by DR EMANUEL MUSKATBLIT and (by invitation) DR L TULIPAN

The patient, a white man aged 65, has been seen at the Clinic of the New York University presenting several types of fungous infection 1 On both cheeks, especially the left one, in front of the ears, there is a faint erythema and scaling of about three weeks' duration Scrapings showed fungi of the ringworm type 2 On the neck there is a faint erythema, scaling and hyperpigmentation of a few weeks' duration 3 The upper middle part of the chest shows erythema, scaling, hyperpigmentation and some lichenification of about two months' duration Scrapings from the left side of the neck and chest showed fungi of the ringworm type 4 On the back there is a brownish scaly patch with numerous brownish macules on the periphery The duration is unknown Examination of the scales showed Malassezia furfur 5 On the left thigh there is a brownish-reddish patch with slight scaling and small foci on the periphery, of ten years' duration Scales from the thigh showed Actinomyces minutissimus and M furfur 6 The soles and lateral aspects of the feet showed scaling The toes and webs showed scaling and maceration of ten years' duration The toe nails showed yellowish and grayish patches and dulness Scrapings from the feet, toes and right big toe nail showed fungi of the ringworm type Cultures were planted with material obtained from areas infected with ringworm

NOTE—The toes showed Trichophyton purpureum All other culture tubes failed to show pathogenic fungi

Pseudopelade (Brocq) (Lupus Erythematosus?) in a Woman Aged 47 Presented by DR ELLEN REINER

Alopecia Cicatrisata (Pseudopelade) in a Negro Woman Aged 38 Presented by DR. LEO SPIEGEL and (by invitation) DR A KORNBLEET

A Case for Diagnosis (Cylindroma? Nevus? Papilliferus Syringadenomatosus? Turban Tumor?) Presented by DR CHARLES WOLF

Charles Wolf, M D, *President*
Henry Silver, M D, *Secretary*
Oct 23, 1947

Mycosis Fungoides, Fungoid Stage, Treated with Antimony Preparations Presented by DR JOHN GARB

D N, a woman aged 49, was registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Jan 17, 1940, presenting lesions of two years' duration The eruption began on the left thigh with a red, nonitchy, oblong patch about 3 inches (8 cm) in diameter Several months later oozing vesicular and crusted patches appeared on the chest and, shortly after, on the neck On the trunk the patches were erythematous and covered with silvery scales and showed minute bleeding points At that time a diagnosis of psoriasis vulgaris was made

On Jan 7, 1942, the microscopic examination of a specimen taken from the left elbow showed chronic eczema

The patient was readmitted to the New York Post-Graduate Hospital on Jan 8, 1943 At that time she presented a generalized erythematosquamous eruption The lesions were sharply marginated, of various sizes and round or oval, and they formed bizarre patches by confluence Most of them were elevated above the level of the surrounding integument and were edematous and infiltrated

In February 1943 a section of a specimen taken from the left forearm was examined histologically by Dr C F Sims The epidermis showed moderate and somewhat irregular acanthosis, with areas of parakeratosis alternating with retained granular layer Moderate intercellular edema and cellular infiltration were visible In the upper part of the corium were numerous small dilated vessels with edematous and thickened walls surrounded by moderate cellular infiltration of a polymorphous character Small round connective tissue cells, epithelioid cells, histiocytes and plasma cells were present In the zone of infiltration there was moderate interstitial and parenchymatous edema The histologic diagnosis was mycosis fungoides

The hemogram was normal, and the eosinophil count, 5 per cent The Wassermann reaction of the blood was negative The sedimentation rate was 10 mm per hour (normal in women, 19 mm per hour), as determined by the Westergren method Tests with old tuberculin elicited negative reactions in dilutions down to 1 5,000 and a plus-minus reaction in a dilution of 1 1,000 The icteric index was normal Roentgenograms of the chest revealed isolated old, calcified, central and parenchymal tubercle scars

During the seven years of observation the therapeutic measures included adequate courses of superficial fractional roentgen radiation exposures, courses of ultraviolet irradiation, and the administration of testosterone, oxophenarsine hydrochloride (mapharsen®) calciferol (vitamin D_2), promin® (sodium p,p'-diaminodiphenylsulfone-N,N'-didextrose sulfonate) intravenously and locally, bismuth subsalicylate, ethyl chaulmoograte, diphtheria toxoid, sodium arsenate, resin of podophyllum, riboflavin, ascorbic acid and anterior pituitary extract

During these years the patient showed no spontaneous remission of any of the lesions There was some temporary regression due to the roentgen irradiation or to some of the other therapeutic agents There was a tendency for most of the lesions to recur in a more aggravated form, and new lesions continued to develop

On April 28, 1947, treatment with antimony potassium tartrate was instituted On May 19, 1947, after ten intravenous injections of 5 cc of a 1 per cent solution of antimony potassium tartrate, given three times weekly, there was spectacular improvement The superficial patches were rapidly undergoing involution, and the raised growths were flattening out

From June 4 to August 8, because of possible toxic reactions, the treatment was changed to triweekly intramuscular injections of stibanose® (the diethylamino ethanol salt of sodium antimony gluconate), 4 cc per dose, the compound being a pentavalent antimony preparation containing 20 mg of antimony per cubic centimeter A total of nineteen injections was given On August 6, the patient was about 80 per cent improved

Electrocardiograms were taken every two to four weeks On August 11 minimal myocardial changes were observed Treatment with stibanose® was discontinued and crude liver extract and thiamine hydrochloride were given

On October 4 the electrocardiogram did not reveal any abnormalities of the ventricular complexes Injections of stibanose® were resumed twice weekly, alternating with administration of liver and thiamine hydrochloride

Examination on October 17 showed that all lesions, except for an isolated few, had completely regressed, leaving faintly superficial, reddish to purplish spots and dark brown patches The breasts, except for two small superficial patches, were entirely clear, the foul-smelling, crusted patches were replaced by normal epidermis A nodular growth on the middle of the left leg remained unchanged

DISCUSSION

DR FRANK E CROSS I should like to ask Dr Garb for the rationale of the use of antimony salts in the treatment of mycosis fungoides

DR JOHN GARB During the past five years I have experimented with many forms of treatment in mycosis fungoides, including promin,® testosterone propionate, diphtheria toxoid, chaulmoogra oil and many others The effect of these measures was only partial and temporary The use of antimony salts was purely experimental, prompted by the success obtained with them in treatment of granuloma inguinale The rapid melting of the ulcerated growth in mycosis fungoides (50 per cent improvement within three weeks) exceeded my expectation

DR CHARLES F SIMS I have examined several sections of specimens obtained in this case One of them presented a pleomorphic cellular infiltration in the upper part of the corium, as well as other histologic changes consistent with the diagnosis of mycosis fungoides

DR SAMUEL M PECK If this is truly a case of mycosis fungoides—and I value Dr Sims' opinion—then the treatment with antimony salts would rank as one of the important contributions to modern therapy It is well known that mycosis fungoides is a type of lymphoblastoma I hesitate to admit that the lymphoblastomatous type of lesion would respond to such a therapeutic measure If the antimony salts really have a beneficial effect on mycosis fungoides, it would be necessary for this disease to be removed from the group of lymphoblastomas I do not believe, however, that antimony salts would have such a beneficial effect on malignant lesions I have treated a variety of dermatoses, principally psoriasis, with antimony salts and have seen such cases clear up after one treatment However, recurrent lesions are resistant to antimony Further trial with antimony salts in treatment of mycosis fungoides is certainly indicated

DR BORRIS A KORNBLITH (by invitation) I have had much experience with antimony compounds, especially in the treatment of granuloma inguinale I have employed antimony potassium tartrate, stibophen (fuadin®), antimony sodium thioglycollate and stibanose® Since granuloma inguinale is a chronic disease and requires a prolonged period of therapy, a number of pertinent observations were possible in evaluating these antimony preparations

It is possible for one to give any of the antimony preparations up to a point of toxicity and to continue with a subtoxic dose for long periods because of the rapid excretion of these compounds through the kidney (for the most part, 80 per cent in twenty-four to forty-eight hours) and through the bowel (10 per cent) For cases requiring larger dosage for maximum therapeutic effect, stibanose® is by far the most advantageous drug There is no pain associated with its subcutaneous or intramuscular administration, while the other antimony preparations, such as antimony potassium tartrate, stibophen and antimony sodium thioglycollate, produce pain when given intramuscularly In general, it may be stated that larger doses of antimony are not possible because of the toxicity of the drug When a less toxic drug is introduced, the larger doses are well tolerated and a better

therapeutic result obtained Initial resistance to antimony, however, is not overcome by increasing the dose

The immediate toxic reactions, in the order of their appearance, are as follows hacking cough, circumoral pallor, blanching of the face, respiration, nausea, retching, vomiting and vasomotor collapse All these symptoms are ameliorated by the prompt use of epinephrine subcutaneously (8 to 10 mm of a 1 1,000 solution) The late symptoms of toxicity are myalgia, especially of the deltoid and the quadriceps femoris muscles, pain along the distribution of the trigeminal nerve, especially in decayed teeth, and cardiac irregularities, such as bradycardia and auricular fibrillation, with occasional electrocardiographic changes

All observations were made on ambulatory patients, who tolerated the antimony drugs in a surprisingly asymptomatic way despite the large doses used

DR JOHN GARB I am in accord with Dr Peck If treatment with antimony preparations should prove effective in other cases of mycosis fungoides, then mycosis *fungoides should be taken out of the group of lymphoblastomas*

Similar remedies, such as chaulmoogra oil, are sometimes used in the treatment of leprosy and of mycosis fungoides It is interesting to note that antimony salts, alone or in combination with arsenic, have been used in the treatment of leprosy, with varying degrees of success, by Kingsbury and others (A New Antimony Compound in the Treatment of Leprosy, ARCH DERMAT & SYPH **24** 1053 [Dec] 1931)

As Dr Kornblith pointed out, the pentavalent antimony preparation stibanose® is the least toxic of all antimony products Nevertheless, toxic reaction, especially myocardial damage, must be guarded against

Keratosis Follicularis (Darier's Disease) *Presented by* DR NATHAN SOBEL

D N, a girl aged 14, presents an eruption which has been present for seven years, but which has become aggravated in the past four years The patient has no brothers or sisters The mother, father and other relatives are not affected by the disease

In both supraclavicular regions and on the sides of the neck there are areas of erythema the size of a palm, with extensive oozing and yellowish crusting The scalp and upper part of the forehead show similar areas There are numerous discrete keratotic lesions the size of a pinhead in the perioral region and also on the neck

Histologic examination on May 3, 1947, showed pronounced hyperkeratosis and an increased granular layer in some areas Classic corps ronds and grains were present in some sections There were lacunas just above the basal cell layer and also within the prickle cell layer in many areas The histologic diagnosis was keratosis follicularis (Darier's disease)

At the clinic the patient received injections of liver extract, potassium arsenite solution (Fowler's solution) and vitamin A by mouth During the summer of 1947 she also had ten intramuscular injections of a preparation containing 100,000 units of vitamin A, given triweekly, with little benefit Since Sept 4, 1947, she has been treated at my office Treatment has consisted of administration of a compound containing 200,000 units of vitamin A daily by mouth in combination with ox bile extract (bile salts) Six roentgen ray treatments were given to the supraclavicular regions and neck There has been moderate improvement However, the patient states that the condition is at its worst in the summer

DISCUSSION

DR NATHAN SOBEL A diagnosis of familial benign chronic pemphigus (Hailey and Hailey) was considered in this case, but the diagnosis of keratosis follicularis was established on the basis of histologic findings The patient is presented because of the failure of the condition to respond to large doses of vitamin A and liver

DR SAMUEL M PECK There are two curious facts that stand out in the treatment of keratosis follicularis with large doses of vitamin A (1) there is a peculiar relation between keratosis follicularis and exposure to light, and (2) some patients who do not respond to oral therapy respond to injections

Exposure to sunlight causes aggravation of the eruption and, at times, vesiculation My patients learn soon enough not to go to the beach It is my experience that lesions on the exposed parts, such as the forehead, face and neck, are more resistant and clear much later than those in comparatively protected areas, such as the axillas It is evident that the light factor plays an important role

Some cases which do not respond to vitamin A therapy alone do respond to treatment with a combination of vitamin A and members of the vitamin B complex This fact was called to my attention by Dr Gross Vitamin B metabolism apparently plays a role in the second factor If some patients do not respond to treatment with vitamin A, it should be supplemented by injections of liver and large doses of nicotinic acid

DR CHARLES R REIN In other cutaneous conditions associated with vitamin A deficiency, the administration of large doses of vitamin A orally did not produce a beneficial effect until absorption from the gastrointestinal tract was implemented by the concomitant ingestion of dilute hydrochloric acid Such a regimen might be effective in treatment of this patient

DR HANS STORCH, Zurich, Switzerland (by invitation) A case of keratosis follicularis recently under observation at the University Clinic in Zurich has responded remarkably well to treatment with grenz rays

DR NATHAN SOBEL With respect to Dr Peck's remarks regarding exposure to light and keratosis follicularis, I can state that this patient's condition had been aggravated during the summer Since it is believed that sunlight has a bad effect *on this condition*, another patient under my observation was kept out of the sun's rays but failed to improve I also exposed a small area of the back of that patient to ultraviolet rays in erythema doses, but no new papules have formed I believe there must be some factor other than sunlight to aggravate the condition during the summer months The patient I presented tonight also failed to improve by avoidance of sunlight She has already been given injections of crude liver extract I shall, however, follow the suggestions of Drs Peck and Rein and try treatment with nicotinic acid and hydrochloric acid I may also try the use of grenz rays, as suggested by Dr Storch

Livedo Reticularis, with Recurrent Superficial Ulcerations of the Feet Presented by DR SAMUEL M PECK and DR KAI K LI (by invitation)

Purpura Annularis Telangiectodes (?). Presented by DRS PAUL GROSS and ELLEN REINER

A Case for Diagnosis (Epidermodysplasia Verruciformis?) Presented by DRS MAX JESSNER and CHARLES R REIN

E W, a man aged 21, presents an eruption of five years' duration It began as a few discrete lesions on the forehead and reached the present stage within a few months The patient has received various types of therapy, including peeling, administration of wart vaccine and roentgen irradiation, with no appreciable change

His parents are nonrelated He states that his older sister has wartlike lesions on the fingers which have persisted for the past several years

The eruption is most conspicuous on the face and consists of discrete, light brown, nonscaly papules varying in size from that of a pinhead to that of a pea Many of these lesions are made up of groups of smaller lesions, some of them taking on an annular configuration The lesions over the bearded portion of the chin are quite characteristic of verruca plana There is a solitary verrucous lesion, the size of a large pea, on the dorsum of the left hand Several of the lesions were destroyed by electrodesiccation and curettage, which resulted in keloidal scarring A lesion of the forehead was removed for microscopic examination Dr C F Sims reported that the epidermis was moderately verrucous There was some elongation and broadening of the rete pegs at many points Considerable vacuolation of the cells of the granular layer and the upper rete cells was observed No noteworthy changes were present in the corium

DISCUSSION

DR EMANUEL MUSKATBLIT The lesions impress me as ordinary verrucae planae What clinical features justify the other diagnosis?

DR HENRY SILVER I hesitate to make a diagnosis of epidermodysplasia verruciformis in this case, but I should definitely rule out verruca plana I admit that the histologic evidence, such as ballooning of the cells and the basket weave appearance of the epidermis, is characteristic These features, however, are not limited to epidermodysplasia verruciformis but are seen in other diseases, such as verruca senilis, mal de Meleda and molluscum contagiosum, and even in common warts We cannot, therefore, rely solely on the histologic evidence Because of our lack of knowledge regarding etiology of the disease, it is difficult and often confusing to separate the clinical varieties encountered These variants of localized or region-specific keratoses are often considered as separate entities on flimsy evidence It is highly probable that epidermodysplasia verruciformis of Lewandowsky and Lutz, Hoffman's verrucosis generalisata and possibly Hopf's acrokeratosis verruciformis are clinical variants of the same disease

The well developed cases of epidermodysplasia verruciformis are readily diagnosed Most of the characteristic features, such as the disseminated, verruca-plana-like lesions, the tendency to malignant transformation, the verruca-vulgaris-like lesions and the verrucous plaque formations, are usually present The case I presented before the Section of Dermatology of the New York Academy of Medicine was a fairly characteristic example of the disease (Epidermodysplasia Verruciformis, ARCH DERMAT & SYPH **45** 836 [Nov] 1941) Dr Rein's case lacks some of the clinical features I would therefore consider his case a forme fruste of the disease

DR PAUL GROSS In spite of the fact that the diagnosis epidermodysplasia verruciformis is still in doubt, I should definitely rule out the suggested diagnosis of verruca plana on clinical grounds

DR DAVID BLOOM From the appearance of the lesions, it is difficult for one to make a diagnosis of epidermodysplasia verruciformis, but one has to favor this diagnosis because of the plaque formation on the face The vacuolation of the epidermal cells seems on histologic examination to support the diagnosis as presented, although such changes are reported also in verruca plana and in other keratotic and dyskeratotic conditions I should like to call attention to the type described in the French literature as *erythrokératodermie verruqueuse en nappes*

DR. CHARLES LERNER In my opinion this is a case of verruca plana, if I may judge from the lesions that I observed on the dorsum of the left hand

DR MAX JESSNER I have little to add to Dr Silver's remarks Dr Rein and I expected a difference of opinion about this case, and for this reason we presented the patient The question of whether epidermodysplasia verruciformis is a dermatosis *sui generis* has become acute again since W Lutz's article appeared in *Dermatologica* in 1946 Epidermodysplasia verruciformis had already once to fight for its existence and nevoid nature when it was confronted with verruca disseminata and verrucosis generalisata, respectively At that time it had, we believed, won the fight Such cases as Lewandowsky and Lutz's first one, which I saw, are impressive, and their nevoid and rather often precancerous nature ought not to be doubted A case not as widespread, with several epitheliomas, shown to me by Dr de Cholnoky, will be presented at a subsequent meeting It is the more or less abortive forms resembling clinically verruca plana which are difficult to diagnose, especially if the vacuolation of the rete cells is not outstanding and because of the fact that a certain degree of vacuolation may also be found in warts In the case presented it is the clinical aspect, especially the confluence of the lesions in some parts of the affected region, and the course of the disease, together with the histologic features, that favor a diagnosis of epidermodysplasia verruciformis

DR CHARLES R REIN I have learned that the patient's sister also had verrucous lesions on the hands If this point is confirmed, it will corroborate the diagnosis as presented The differential histologic diagnosis lies between verruca plana and epidermodysplasia verruciformis The clinical findings, history and course of the condition must be taken into consideration before a definite diagnosis can be established

Parapsoriasis Varioliformis Presented by DR FRANCES PASCHER

Juxta-Articular Nodes in a Patient with Neurosyphilis Presented by DR JULIUS H POLLOCK

Basal Cell Epithelioma of the Nipple of a Man Presented by DR NATHAN SOBEL

L S, a man aged 46, has been a patient at the Skin and Cancer Unit of the New York Post-Graduate Hospital since Sept 19, 1947 The duration of the lesion is not definitely known, but the condition has been present for at least several years When the patient was first seen at the hospital there was in the area of the right nipple a scaly and somewhat crusted noninflammatory lesion the size of a dime The diagnosis of carcinoma simplex (Paget's disease) of the nipple was considered At present the entire right nipple and adjoining areola show an infiltrated plaque with an irregular surface

The Wassermann reaction of the blood was negative on Sept 19, 1947 Microscopic examination made by Dr C F Sims, showed that the epidermis was eroded

in one area Below it there was a large mass made up of groups and strands of basal cells The palisade layer was intact There was a slight inflammatory infiltrate in the midcutis

DISCUSSION

DR CHARLES F SIMS I have examined the slide, and there is no question that it is of basal cell carcinoma

DR HENRY SILVER I suggest that the condition be subjected to the Mohs method of therapy

DR FRANK E CROSS Cancer of the breast in the male is more malignant than is that in the female It is rather uncommon in the male and is usually of the prickle cell type I do not question the histologic report, but in view of the previous statement I feel that one must be more radical in therapy I should, therefore, suggest a wide excision of the nipple, followed by the making of serial sections of the specimen removed for further histologic study

DR CHARLES F SIMS Dr Cross's suggestion of a possible prickle cell epithelioma was not substantiated by the histologic findings

DR NATHAN SOBEL When first seen the lesion was scaly and crusted, and the diagnoses that were considered were chronic eczema, possibly Paget's disease and keratosis of the nipple Tonight the lesion looks clean and somewhat nodular, and it is difficult to make the diagnosis on clinical grounds alone

As Dr Cross stated, basal cell epithelioma of the nipple in the male is a rare condition Dr Arthur Hyman reviewed the literature and could find only the following references to its occurrence Elliott and Welland (ARCH DERMAT & SYPH **53** 322, 1946) reported not a single case of basal cell epithelioma of the nipple among 1,928 cancers of the skin In 1924, Wainright (*Arch Surg* **14** 844, 1927) reviewed 264 cancers of the male breast and found only 1 case of basal cell epithelioma in the series In this series there were only 6 prickle cell epitheliomas, so even prickle cell epithelioma of the nipple is rare Geschickter (Diseases of the Breast, Philadelphia, J B Lippincott Company, 1943, p 603) refers to a reported case of basal cell epithelioma in the female breast mentioned by Ewing Dr Hyman informed me that he has personally seen 1 case of basal cell epithelioma of the male nipple and adjoining areola which was clinically diagnosed as Bowen's disease

After the lesion is removed, serial histologic sections will be studied

FOLLOW-UP NOTE Serial sections showed only basal cell epithelioma

Multiple Pigmented Nevi Presented by DR CHARLES WOLF

Poikiloderma of Civatte Presented by DR HARRY B FEILER

PHILADELPHIA DERMATOLOGICAL SOCIETY

J M Schildkraut, M D, *Chairman*

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April 18, 1947

Herpetic Stomatitis and Vaginitis (Pemphigus?) Presented by DR JOHN F WILSON

Scleroderma with Calcinosis Presented by DR CARMEN C THOMAS and (by invitation) DR DAVID KREMER

Blastomycosis with Pulmonary Involvement. Presented by DR CARMEN C THOMAS and (by invitation) DR G H WELLS

Cutaneous Diphtheria Presented by DR CLARENCE S. LIVINGOOD and (by invitation) DR HARVEY BLANK

C L, a white man aged 25 years, presents healed, round scars on both legs, approximately 1 inch (2 cm) in diameter, with brownish, pigmented, atrophic centers On July 10, 1944, five weeks after the patient's arrival in Burma, ulcers appeared on both legs On August 3 he was admitted to the 69th General Hospital, Assam, India, with multiple, punched-out ulcers with a tough black eschar and a rolled bluish red border On October 1 numbness and weakness of the fingers, toes, hands and feet appeared By October 31 the skin had healed, and by December 30 the neuritic symptoms had cleared

The smears taken from the ulcers did not show fusiform bacilli or spirochetes Cultures were not available, but virulent Corynebacterium diphtheriae were cultured from many other patients with the same type of lesion

The patient was treated with various bland local measures and bed rest As the result of his Schick test was negative, no antitoxin was given

DISCUSSION

DR CLARENCE S LIVINGOOD This is a patient whom Dr Blank saw from the onset of his illness The scars are typical postdiphtheritic ones Other ulcerative lesions can leave scars, but with experience one can identify the postdiphtheritic type We had difficulty in convincing our colleagues that cutaneous diphtheria produced ulcers that are diagnostic Any dermatologist who is accustomed to seeing and making fine distinctions between ulcerative lesions can make this diagnosis without difficulty Anthrax, first degree burns and trophic ulcers can produce somewhat similar scars, but I do not believe that any other conditions produce ulcers of this type

A Case for Diagnosis (Poikiloderma Atrophicans Vasculare?). Presented by CAPTAIN ROBERT L GILMAN, United States Navy

Parapsoriasis en Plaques Presented by DR LEWIS M JOHNSON

R J, a white man aged 19 years, noticed an eruption on his lower extremities shortly after an attack of severe bronchitis in the spring of 1945 There have been no subjective symptoms The lesions started as small macules and gradually progressed in size and number and occurred on his upper extremities together with an associated loss of pigment During the summer of 1946 the eruption on his upper extremities faded considerably, but recurred during the past winter The history reveals no prolonged ingestion of drugs prior to the onset of the eruption except for "drops" for his heart The patient is well built and presents variously sized, round and oval, pinkish to copper-colored, macular lesions, some of which have a fine scale and a reticulated appearance They are more profuse on the lower extremities, those on the upper extremities have an associated patchy loss of pigment in the surrounding skin These lesions, when viewed with filtered ultraviolet rays ("black light"), are darkened and more pronounced on the lower extremities and have a faint fluorescence on the upper extremities The results of the rest of the physical examination were essentially normal except for a soft mitral systolic murmur, a chronic macerated and fissured eruption between the toes of both feet and hyperhidrosis of the hands and feet

A complete blood cell count revealed 93 per cent hemoglobin (14 73 Gm), 4,870,000 erythrocytes, 11,600 leukocytes, 71 per cent polymorphonuclear leukocytes and 29 per cent lymphocytes The result of the Kline test of the blood for syphilis was negative The potassium hydroxide preparation of the scales did not reveal fungi A urinalysis showed no abnormalities

DISCUSSION

DR MEYER L NIEDELMAN I suggest the diagnosis of erythema multiforme perstans The lesions have been present for two years, are sharply marginated and on diascopic pressure become rather light, and the surrounding tissue seems to have some pitting edema

DR FRITZ CALLOMON (by invitation) The diagnosis of parapsoriasis appears acceptable This form corresponds to Brocq's erythrodermie pityriasique en plaques disseminees and the yellowish color with the English description of Radcliffe Crocker's xanthoerythroderma perstans Although the lesions of Brocq's disease usually persist unchanged over many years, seasonal changes were observed by Civatte, White and Brocq himself, who described obvious remission during the summer and exacerbation during the winter months (Jadassohn, J Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol 7, pt 1, p 388)

DR BERTRAM SHAFFER This eruption has a peculiar artificial appearance I suggest the diagnosis of factitial eruption The lesions are sharply demarcated and regular, and all of them are disposed on parts of the body accessible to the patient

DR DONALD M PILLSBURY I agree with Dr Shaffer The pharyngeal and corneal reflexes are absent Some of the lesions have disappeared, which is against the diagnosis of parapsoriasis If it turns out that the patient has parapsoriasis, I suggest a trial of anthralin to the point where it produces some reaction This case is similar to one Dr Kulchar had in our clinic some years ago, the only one of parapsoriasis which cleared up with treatment with anthralin (dihydroxyanthranol)

DR LEWIS M JOHNSON, Lancaster, Pa I cannot agree that the patient produced the lesions on the backs of the arms, nor can I understand the depigmentation I thought of a fixed type of eruption when I saw him first in November I shall let you know the report of the biopsy

NOTE—The diagnosis from the biopsy was parapsoriasis (Lancaster General Hospital)

Sporotrichosis Presented by DR J M SCHILDKRAUT, Trenton, Pa

Recurrent Lupus Erythematosus Presented by DR H E TWINING

J C, a Negro man aged 30 years and well nourished, presents sharply marginated, eczematous, slightly scaly patches of dermatitis on the cheeks, nose and mucous membranes of the mouth of about four months' duration The original lesions almost completely disappeared with treatment with bismuth subsalicylate injections and liver This is the third recurrence, all the lesions appearing at the original sites A small, erythematous area developed on the bridge of the nose in 1943 This was diagnosed as eczema Three months later it recurred with erythematous scaly lesions sharply demarcated on the nose and cheeks

A roentgenogram of the chest did not show tuberculosis Treatment with injections of bismuth compound and liver was successful in previous attacks but produced no improvement in the present one

DISCUSSION

DR CHARLES R REIN, New York (by invitation) I have used bismuth sodium triglycollamate (bistrimate®) in a number of conditions, including lupus erythematosus, lichen planus, verruca and granuloma annulare Best results were obtained in patients with lupus erythematosus Two patients with this condition showed no improvement after many intramuscular injections of bismuth subsalicylate but responded well to oral treatment with bismuth sodium triglycollamate This preparation was also efficacious in some patients with acute generalized lichen planus, but the results in the other diseases were disappointing

DR H E TWINING I tried bismuth sodium triglycollamate in this patient but had to discontinue it because of the occurrence of stomatitis and gingivitis Has Dr Wright seen many patients who cannot tolerate this drug?

DR CARROLL S WRIGHT My co-workers and I have the same percentage of intolerance with this preparation as with bismuth given in any other form

DR MEYER L NIEDELMAN At the last Atlantic Dermatological Conference suramin sodium (naphuride®) was mentioned for the treatment of lupus erythematosus It would be worth while to try it in this patient, if bismuth preparations prove ineffective

DR STEPHEN WHELAN (by invitation) In a total of about 25 patients with discoid lupus erythematosus my co-workers and I have used bismuth sodium triglycollamate in the past year and a half and we have not had the favorable results that Dr Wright and Dr Gross have reported We had 2 cases of hypertrophic lichen planus with good results in which the disease had not responded to bismuth compound administered intramuscularly

Multiple Large Keloids. Presented by DR MEYER L NIEDELMAN

E R, a white man aged 25 years, has a large, thick, keloidal band on his neck It is lobulated and adherent and limits the motion of the chin There are a number of small keloids on the cheek, chest, back and arms and on the vaccination site There are no lesions on the lower extremities On the forehead, cheeks and nose there are numerous hyperpigmented macules from pinpoint size to pea size, which the patient stated have been present since birth He had a burn from hot water on the neck at the age of 8 years, the past history is otherwise normal At the age of 12 the patient first noticed the keloids about the neck Shortly thereafter papules developed on the right side of his face, which subsequently developed into keloids He sustained a human bite on the sternal area at the age of 16, which developed into a keloid

In 1943, at another institution, the entire keloid on the neck was surgically removed, sutured and treated with roentgen rays This region shortly grew larger than the original In 1944 the keloid on the left side of the neck was similarly treated, that on the right side of the neck was operated on in September 1944, with a skin graft from the right thigh A keloid developed at the donor site

DISCUSSION

DR. J P SCULLY (by invitation) This patient shows two different types of scar The question arises whether endocrine disturbances are a factor in the production of keloidal change and whether, if further surgical attempts were made in this case, it might be well to attempt the coincident injection of diethyl

stilbestrol or male sex hormone during the postoperative period It was suggested that one lesion, possibly the one on the sternum, be excised in trial treatment and then some type of therapy determined In one case irradiation was suggested I should like to see diethyl stilbestrol or some similar preparation tried in order to determine whether the keloidal aftermath might be prevented

DR IRA L SCHAMBERG Are keloids ever seen before puberty? Children suffer all sorts of trauma, and, if they are not seen, Dr Scully's suggestion has some merit

DR DONALD M PILLSBURY I have seen many keloids in children

DR MAX JESSNER, New York (by invitation) I had a keloid when I was a small boy, but not since then Keloid formation is due to a "fibrotic" tendency of the organism, and that may change I do not believe that we know the reason for this, but many things have been suggested There has been a report by a physician who cured keloids by the administration of sodium fluoride (Callam, M *Munchen med Wchnschr* **82** 1534, 1935) I tried it in a case and had the impression that it did good I was afraid, however, to give it in large doses

CAPTAIN ROBERT L GILMAN, United States Navy I have seen keloids in children 4 to 8 years of age

DR THOMAS BUTTERWORTH, Reading, Pa Keloids do occur in children I am treating a keloid now in a youngster The statement occurs in some books that keloids tend to undergo involution after the menopause I have seen a keloid develop in the breast of a school teacher about 55 years of age For the case presented today I recommend Dr H J Smith's 2 per cent menthol in cottonseed oil with massage

DR DOUGLASS A DECKER, Allentown, Pa Dr Smith stated that the menthol and cottonseed oil preparation helps only those patients with itching or pain in the keloid

J M Schildkraut, M D, *Chairman*

Douglass A Decker, M D, *Secretary*

May 16, 1947

Psoriasis, with Extensive Koebner Phenomenon Induced by Systemic Reaction to Sulfadiazine Applied Locally to Burn Presented by DR LESLIE NICHOLAS and (by invitation) CAPTAIN RAYMOND R SUSKIND

Trichophyton Purpureum and Monilia Infection of the Hands, Feet and Nails Moniliasis of the Tongue Presented by DR LESLIE NICHOLAS and (by invitation) CAPTAIN RAYMOND R SUSKIND

Pigmented Purpuric Lichenoid Dermatitis Presented by DR LOUIS GOLDSTEIN

S W, a white man aged 29 years, presents on both legs many smooth, small, slightly elevated papules, some of which fuse into poorly marginated patches They are reddish brown The condition began about six months ago on the latero-anterior aspect of the left leg as a reddish, flat, papular, quarter-sized lesion with no subjective symptoms and gradually progressed to the present size

DISCUSSION

DR FRED D WEIDMAN I think we were all struck by the extremely lurid color of these lesions, in six months there certainly ought to be some pigmentation, yet there is not In the sections there is not any sign of hemorrhage to explain the extreme redness nor is there any pigment One must explain the redness on some other basis than that, and it is known that sometimes infiltrations of cells will produce a red color, for example, the small red kidney in chronic interstitial nephritis There is not any particular vascular hyperplasia, and there is no hemorrhage, but there is something different in the constitution of the cells which in the aggregate makes them red That was one of the things that puzzled me in this case Microscopically certain features suggest lichen planus, like the sharp demarcation of the zone underneath, but cellular infiltration is sparse for that, considering that these are fresh lesions, yet they are so highly elevated and delicately nodular or papular They are not in a regressive stage They are not atrophic lesions If this were lichen planus it would have to be atrophic lichen planus, and that is contrary to what this patient presents There are many histiocytes, and I do not know what the significance of those may be except that they tend to assist in eliminating lichen planus as a diagnosis The grouping is not discoid, as it should be in Majocchi's disease, and the lesions are not hemorrhagic In this type there should be some pigmentation There is a slight scaliness, but in the Gougerot-Blum complex I think that there should be more scaliness than is shown here I think that this is a puzzling case, and I cannot give a specific diagnosis

A Case for Diagnosis (Leukemia?) Presented by DR THOMAS BUTTERWORTH, Reading, Pa

Extensive Verruca Plantaris, Verruca Vulgaris Presented by DR J M SCHILDKRAUT, Trenton, N J

DISCUSSION

DR C S LIVINGOOD I suggest that the patient soak his feet daily in a solution of formaldehyde It is well to use 4 per cent formaldehyde for only a minute or so at first and gradually increase the time to four or five minutes, depending on the reaction

DR THOMAS BUTTERWORTH, Reading, Pa I often advise patients to apply 60 per cent salicylic acid paste and bandage the foot for about three days and then rub in 30 per cent salicylic acid paste nightly with the round head of a clothes pin, this seems to be effective

DR ISADORE ZUGERMAN Has the patient had bismuth sodium triglycollamate?

DR J M SCHILDKRAUT, Trenton, N J He has had bismuth subsalicylate injections

DR THOMAS BUTTERWORTH When treating a patient with formaldehyde solution, one must be sure that the fluid is not much more than a ¼ inch (0 64 cm) deep

Tuberculosis Verrucosa Cutis Presented by DR SIMON KATZ and (by invitation) DR PETER HORVATH

Trichophytosis Barbae Presented by DR M H SAMITZ and (by invitation) DR LAWRENCE KATZENSTEIN

Pityriasis Rubra Pilaris Presented by DR CARROLL S WRIGHT and DR MEYER L NIEDELMAN

E F, a Negro woman aged 39 years, first had a severe sore throat and a painful right shoulder about two months ago She used a gargle several times daily, consisting of a solution of 1 teaspoonful of salt and several drops of iodine About two weeks ago swelling of the face, puffiness of the eyes and scaling of the scalp developed The eruption on the arms and body followed After the eruption appeared she received several injections of an unknown substance There is an acute inflammatory dermatitis of the face and edema of the periorbital areas with pronounced conjunctivitis The scalp and other hairy areas show scaliness On the extensor surfaces of the arms, shoulders, nucha and legs is a widespread discrete follicular keratotic eruption There is little itching There is no history of ingestion of drugs The Wassermann reaction of the blood for syphilis was negative

DISCUSSION

DR. HERMAN BEERMAN This is lichen planus

DR STEPHEN T WHELAN (by invitation) Some manifestations of the disease are incompatible with the diagnosis of lichen planus The process began on the face with edema and scaling, shortly after the patient had been to the hair dresser She also has scaling on her palms This is an allergic reaction to something that has been applied to the patient's hair

DR. C S LIVINGOOD Both Dr Beerman and Dr Whelan are right The patient has a Koebner phenomenon at the sites of her shoulder straps She may have both contact dermatitis and lichen planus

DR MEYER L NIEDELMAN Pityriasis rubra pilaris may have an acute explosive onset, it may start on the scalp and travel to the face I believe that this is a case of pityriasis rubra pilaris with a sudden and acute onset The patient has had no medication and has gone to the beauty shop many times before, with no ill effect The plugs and the involvement of the hairy areas are in accord with that diagnosis

DR D M SIDLICK I do not recall seeing in any reports or textbooks pityriasis rubra pilaris characterized by lichenoid lesions, and, if this is such a case, we shall have to change our concept once again

DR FRED D WEIDMAN There is a condition known as lichen planopilaris, maybe that would reconcile the different diagnoses that have been advanced In the histologic sections it was found that the lichen planus changes do extend down around the hair follicles, making them unduly prominent At the Naval Hospital there was a patient who had a patch of hypertrophic lichen planus on the thigh, and in one there were definite pits, which made me think at first of those which occur when one pulls out a plug from a lesion of Darier's disease These were located at the orifices of hair follicles I would suggest that the patient be examined with respect to a diagnosis of lichen planopilaris, which would bridge the two separate diagnoses advanced

DR LOUIS GOLDSTEIN I thought that lichen planopilaris had to do with the scalp and not with the glabrous parts of the body

DR. HERMAN BEERMAN The typical lesions of lichen planopilaris do occur on the wrists usually

NOTE—Microscopic examination of a biopsy specimen by Dr Fred D Weidman and by Dr Ernest Regertis resulted in a diagnosis of pityriasis rubra pilaris

Scleroderma in an Infant. Presented by DR J. M. SCHILDKRAUT, Trenton, N J.

A B, an infant 1 week of age, has had an eruption on the back since birth Examination shows hard, infiltrated plaques on the upper part of the back, anterior aspect of the chest and the right cheek

DISCUSSION

DR. CARMEN C THOMAS I suggest the diagnosis of subcutaneous fat necrosis of the newborn The lesions were present at birth, after a difficult labor lasting a day and a half, with delivery finally accomplished by forceps The lesions are deep seated, with the periphery beginning to show gradual involution

DR D M SIDLICK Scleroderma in an infant 1 week old would be accompanied by clinical evidence of systemic involvement The tense, edematous skin as well as the distribution and its presence since birth are more in consonance with the diagnosis of scleredema than scleroderma

DR FRED D WEIDMAN I offer an alternative diagnosis of lipophagic granuloma

DR J M SCHILDKRAUT, Trenton, N J Dr Klauder thought that the patient had scleroderma

DR H H PERLMAN I have seen a good many cases of so-called subcutaneous fat necrosis in the newborn The condition is usually described as sclerema neonatorum by many writers (misnomer) The mother stated that she had had an unusually difficult and prolonged labor It is for this reason that trauma should seriously be considered as a causative factor The condition appears a few weeks after birth and invariably disappears spontaneously, usually after a few months Someone mentioned sclerema neonatorum I do not think that this is a case of sclerema neonatorum, because that is a congenital condition or appears soon after birth (usually between the second and tenth day after birth) The condition affects the lower extremities and then spreads to the trunk In sclerema neonatorum, on pressing the affected sites one gets the impression that one is prodding the skin of a cadaver, the skin feels like half-frozen tissue Most patients with such a condition die early The lesions are rather extensive in this case, which is strongly in favor of subcutaneous fat necrosis If this is not a case of subcutaneous fat necrosis, then I would endorse the diagnosis of scleroderma

Reuben Friedman, M D, *Chairman*

Douglass A Decker, M D, *Secretary*

Sept 19, 1947

Multiple Benign Cystic Epithelioma in a Girl Aged Eight Years. Presented by DR LEWIS M JOHNSON, Lancaster, Pa

A Case for Diagnosis (Angioma?). Presented by DR JOHN F WILSON

A J, a white woman aged 49 years, has a group of small red papules in the middle of the flexor surface of the left forearm The color can be pressed from the lesions, and the intervening skin is erythematous In August 1945, the patient had an appendectomy and right oophorectomy for simple ovarian cyst and appendicitis In April 1947, an exploratory laparotomy and transverse colostomy

were performed for postoperative adhesions and diverticulitis of the middle part of the sigmoid In August 1947, resections of the sigmoid were done for adenocarcinoma with metastasis to the regional lymph nodes The patient noticed a small red spot in the middle of the left forearm a year ago This remained about the same until May 1947 After an exploratory laparotomy the lesion spread, the present eruption has existed for several months

A blood cell count revealed 78 per cent hemoglobin, 4,300,000 erythrocytes and 6,000 leukocytes The urine was normal The Wassermann and Kahn reactions of the blood were negative The blood urea nitrogen was 13 2, plasma proteins 6 15, albumin 4 29 and globulin 1 9

DISCUSSION

DR FRED D WEIDMAN I think that it is necessary to see the sections for the diagnosis They show clearly the structure of a capillary angioma It is not a solitary large tumor, but there are microscopic puncta in the tissues The neoplasm is scattered throughout the section There is a good deal of hyperplasia of the endothelium More of the epithelium seems to comprise the bulk of the lesion than the blood vessels Perhaps that is why the lesion does not appear to be particularly red The patient has had this, I understand, for five years, which would point to the diagnosis of angioma rather than angiosarcoma A general pathologist from the sections might diagnose this as an angioendothelioma proliferating into the surrounding tissue, but dermatologists know that there are other lesions, such as granuloma pyogenicum and dermatofibromas, which appear to be infiltrative and yet do not have the neoplastic property of a true malignant condition I should say that these are capillary angiomas rather than angiosarcomas

Pityriasis Rosea? Neurofibromatosis Presented by DR EVAN B HUME

DISCUSSION

DR EVAN B HUME Why is neurofibromatosis aggravated by pregnancy?

DR BERTRAM SHAFFER Many conditions either develop or become aggravated during pregnancy Cutaneous tags, various pigmentations, verruca senilis and von Recklinghausen's disease belong to this group of eruptions

DR SIGMUND S GREENBAUM I offer the diagnosis of a mixed type of anetoderma None of the lesions look like pityriasis rosea The larger lesions resemble Schweninger-Buzzi disease

DR REUBEN FRIEDMAN I agree with the diagnosis of pityriasis rosea and von Recklinghausen's disease Dr Cipollaro of New York is opposed to biopsies in frank cases of neurofibromatosis, stating that in 13 per cent of the cases sarcoma develops at the site of the biopsy

Lupus Erythematosus, Scleroderma (Sclerodactylia), Raynaud's Disease, Sarcoidosis (Boeck's?) Presented by DR LEWIS M JOHNSON, Lancaster, Pa

Keratoses of the Palms and Soles (Chronic) (Caused by Arsenic?), Pigmentation (Generalized) (Caused by Arsenic?), Dermatitis (Atopic) of the Hands, Forearms, Ankles and Popliteal Areas (Chronic), Cirrhosis (Portal) of the Liver (Chronic) (Cause Undetermined) Presented by DR LESLIE NICHOLAS and (by invitation) CAPTAIN A FRISKEL

Tuberculosis of the Skin. Presented by DR H A. LUSCOMB for DR FRANK C KNOWLES

T C a Negro woman aged 21 years, presents a generalized, lichenoid, umbilicated, papular eruption with condylomata lata on the external genitalia The patient was admitted to the clinic in January 1947, with a history of an eruption of two months' duration

The Wassermann and Kahn reactions of the blood were strongly positive A blood cell count and the results of urinalysis were normal The serum calcium was 11 2 Roentgenograms showed the chest, hands and feet normal The result of a tuberculin test performed on April 1 with purified protein derivative (first and second test dilutions) was negative

The diagnosis from biopsy was tuberculosis

Antisyphilitic treatment with oxophenarsine hydrochloride was begun on Jan 17, 1947 The condylomata disappeared, but the rest of the eruption remained the same after three months' treatment Calciferol (vitamin D_2) therapy, 100,000 units daily, was started on May 31 and continued to the present time The eruption on the face had disappeared in six weeks The rest of the eruption has slowly improved

DISCUSSION

DR D M SIDLICK Only the microscopic evidence is in favor of tuberculosis of the skin, and I do not believe that one can make a diagnosis merely on the basis of the histologic picture The clinical evidence favors syphilis, and this is a macular atrophy following secondary syphilis

DR FRED D WEIDMAN This might be a case of sarcoid in the form that occurs in the American Negro, which responds to vitamin D_2 therapy The sections suggest sarcoid, although there are many lymphocytes, there are no giant cells The patient is anergic, but the other lesions, such as the bone changes, appear not to be present The disease is, however, in an early stage, and I think that the case should be watched because it may be one of sarcoid of the American Negro, which Dr Michelson thinks might be different from sarcoid of Boeck

DR C C THOMAS I have seen at least three examples of what appeared to be papular secondary syphilis which on further examination and failure to respond to antisyphilitic therapy turned out to be sarcoid I suggest a lymph node biopsy

Purpura Annularis Telangiectodes (?) Improved Following Treatment with Rutin and Ascorbic Acid Presented by DR SIGMUND S GREENBAUM

Follow-Up Report Presented by DR J M SCHILDKRAUT, Trenton, Pa

Some time ago I reported an extensive case of plantar warts—one of the worst I had ever seen The boy had an extensive case of fused warts on the whole anterior part of the foot and scattered warts on the heel and toes, he also had warts on his hands He had received roentgen rays, bismuth preparations and other medicaments without effect I gave him a course of bismuth injections and advised that he soak his foot, at the suggestion of Dr Livingood, in 3 per cent formaldehyde, and the condition cleared up

Reuben Friedman, M D, *Chairman*

Douglass A Decker, M D, *Secretary*

Oct 17, 1947

A Case for Diagnosis (Psychosomatic Dermatitis? Dermatitis Herpetiformis?) Presented by DR REUBEN FRIEDMAN and (by invitation) DR CONRAD STRITZLER and DR JOHN B ROXBY JR

Xanthoma Eruptivum Secondary to Lipid Nephrosis Presented by DR REUBEN FRIEDMAN and (by invitation) DR WALDO E NELSON, DR CONRAD STRITZLER and DR JOHN B ROXBY JR

Combined Simple and Cavernous Angioma Presented by DR MEYER L NIEDELMAN

D A, a white girl aged 2 months, presents over the entire left side of the face an angioma cavernosum It is bright red, and the prominence of the swelling lies over the parotid gland There are numerous both raised and flat simple hemangiomas scattered over the right side of the face and neck On the lower lip there is a similar lesion

A small red area developed in front of the left ear at 2 weeks of age Another lesion formed on the lower lip, then gradually new areas developed over the left and right sides of the face and neck The patient was seen two days ago, and arrangements are being made to treat the lesions with radium

DISCUSSION

CAPT R L GILMAN, U S N This patient should be treated with sclerosing injections or solid carbon dioxide I would not use radium or roentgen rays

DR MEYER L NIEDELMAN I am afraid to use sclerosing solutions about the scalp and face because of possible thrombosis of a cerebral vessel At a meeting of the American Academy of Dermatology and Syphilology a few years ago a case was reported in which death of an infant was due to the injection of a sclerosing solution for an angioma of the face I believe the cosmetic result would be poor with solid carbon dioxide, and this substance is ineffective in the cavernous type I shall use radium, and I am sure a regression of the angioma will take place

DR H E TWINING The more rapid the growth, the greater the response one gets from radium or roentgen rays

DR M H SAMITZ I suggest that a roentgenogram be taken of the face to see whether there is any involvement of bone

DR THOMAS BUTTERWORTH, Reading, Pa Frequently extensive hemangiomas occurring in the trigeminal area are accompanied with hemangiomas of the cerebral cortex, and in treating them with roentgen rays one exposes oneself to a medicolegal proceeding If cerebral lesions develop later, the patient's parents may ascribe them to the treatment given earlier At the age of 12 or 14 the angioma on the cortex of the brain may become calcified and can be demonstrated by roentgenogram

DR HERMAN BEERMAN What is "simple" angioma?

DR MEYER L NIEDELMAN There are two types present in this infant the small, flat type, which is simple, and the elevated, doughy, vascular type, which is cavernous

DR J M SCHILDKRAUT Port wine stains are notorious for their failure to respond to roentgen rays But Dr Pfahler and I have recently had infants with such lesions that did respond and we are of the opinion that if radiation is used early these lesions may respond

Sarcoid Solitary Lesion on the Nose Presented by DR CARROLL S WRIGHT and DR E R GROSS

Acne and Comedos in an Infant 8 Weeks of Age Presented by DR. H H PERLMAN

Tuberculosis Verrucosa Cutis on the Neck. Presented by DR MEYER L NIEDELMAN

Reuben Friedman, M D, *Chairman*

Douglass A Decker, M D, *Secretary*

Nov 21, 1947

A Case for Diagnosis (Cutaneous Diphtheria?) Presented by DR LEWIS M JOHNSON (Lancaster, Pa)

A M B, a white woman aged 28, presents a healing ulcer in the right lower quadrant of the abdomen, early necrotizing lesions on the inner side of the left thigh of three days' duration and numerous depressed scars on the left wrist, on the left breast, in the left groin, on the left leg and on the left side of the abdomen She also has a tumor on the left lower part of the back

The present condition developed on Oct 12, 1946, with a "red spot" on the left wrist which formed a blister, turned black, ulcerated and healed, leaving a deep scar Since then other similar lesions have developed When the ulcers develop, she sometimes has painful joints, malaise, nausea and severe menstrual cramps

The serologic tests for syphilis were negative A complete blood count revealed 76 per cent hemoglobin, 3,620,000 erythrocytes, 7,200 leukocytes, 75 per cent polymorphonuclear leukocytes, 23 per cent lymphocytes, 1 per cent monocytes and 1 per cent eosinophils

The microscopic examination of the biopsy section revealed a focus of incomplete necrosis involving essentially the stratified squamous epithelium and its immediate underlying connective tissue This reaction was associated with an inflammatory cell infiltration consisting essentially of eosinophils, plasma cells, lymphocytes and a few polymorphonuclears (neutrophils) This infiltrate occurred chiefly about the blood vessels in the subepithelial areas In some areas the walls of the blood vessels showed a similar infiltration There was also a granulomatous reaction resembling a foreign body reaction Numerous foreign body giant cells appeared in these lesions, and in many instances they contained greenish crystals New blood vessel formation was a prominent feature and appeared to be demarcating the area of necrosis The diagnosis was necrosis of the skin

DISCUSSION

DR CLARENCE S LIVINGOOD This could be cutaneous diphtheria. It might be a factitial eruption caused by an escharotic chemical, such as phenol or saponated cresol solution, but from a clinical standpoint the most likely diagnosis

is cutaneous diphtheria The patient has numbness and tingling of her hands and some weakness She had a severe sore throat about two months after the first lesion developed I suggest careful bacteriologic studies on the most recent lesion, done with the full realization that it is difficult to isolate the Klebs-Loeffler bacillus from the skin even when it is present A spinal fluid examination should be done, and if the patient has an elevated spinal fluid protein, it would lend weight to the thought that the numbness and tingling of the hands represent a neurologic complication of the cutaneous diphtheria

DR DONALD M PILLSBURY I saw this patient after Dr Livingood did, and our initial joint reaction was that culture for corynebacterium diphtheriae was indicated The usual sharp borders of a factitial eruption produced by an escharotic are also characteristic of many diphtheritic ulcers of the skin, and the differentiation may be difficult I suggest, in addition, very careful clinical study from the standpoint of peripheral neuritis or other late changes due to diphtheria toxin If any further collateral evidence of diphtheria is uncovered and if a factitial origin can be ruled out, I suggest administration of diphtheria antitoxin, even if the cultures are negative As has been pointed out, recovery of the organism may be difficult in the hands of even the most experienced bacteriologist, especially when the lesion is old or when local treatment, such as applications of penicillin, has been given

Sulzberger-Garbe Disease (?) (Exudative Discoid and Lichenoid Dermatosis) Presented by DR LOUIS GOLDSTEIN and (by invitation) DR J FERNANDEZ

H K, a white man aged 43, presents papulomacular eruptions on the trunk and extremities which are retiform in character The papules are large, flat topped and reddish-yellow or darker, with mild scaling The patient has had attacks of this condition since 1930 He was hospitalized in April 1947 for an intensely pruritic dermatosis of several months' duration He was discharged much improved after three weeks of treatment Several days after discharge the dermatosis recurred, and he was again hospitalized for five weeks and was discharged much improved Several days later the condition recurred again, and it has remained until the present time

A urinalysis showed occasional leukocytes, epithelial cells and some mucus Complete blood counts revealed 3,890,000 to 4,060,000 erythrocytes, 10,000 to 14,000 leukocytes, 60 to 82 per cent polymorphonuclear leukocytes, 16 to 33 per cent lymphocytes, 1 to 2 per cent monocytes, and 8 to 15 per cent eosinophils The blood sugar was 99 mg per hundred cubic centimeters of blood The urea nitrogen was 13 5 mg The serologic tests for syphilis elicited negative reactions On April 21, 1947, Dr Weidman reported the biopsy specimen to show psoriasis

The patient has been treated with coal tar solution N F, boric acid, amobarbital sodium (sodium amytal®), tripelennamine hydrochloride (pyribenzamine hydrochloride®), protein hydrolysate, starch baths and bismuth sodium triglycollamate (bistrimate®), with improvement

DISCUSSION

DR CHARLES R REIN, New York (by invitation) I agree with the diagnosis

DR MAX JESSNER, New York (by invitation) This condition was unknown in Europe but I have seen many cases in New York I suggest that the patient be treated with arsenic or be sent to Arizona, where most of these eruptions clear up

DR STEPHEN T WHELAN What type of arsenic does Dr Jessner use?

DR MAX JESSNER, New York (by invitation) I inject a 1 per cent solution of arsenic trioxide with 2 per cent phenol, starting with 0 25 cc daily and increasing to 1 cc daily

DR CLARENCE S LIVINGOOD I have no better diagnosis to offer than Sulzberger-Garbe disease, but I always feel dissatisfied with that diagnosis This patient is similar to one of mine whose eruption cleared up, partly because of hospitalization and partly because of therapy of various types The most notable thing about his course was that there would be a flare-up following an infection of the upper respiratory tract or the injection of an autogenous vaccine in a very small dose

Mycosis Fungoides Presented by DRS CLARENCE S LIVINGOOD and (by invitation) J P SCULLY

W B, a white man aged 82, was first seen on Oct 7, 1947, with the chief complaint of "sore on the back" which had been present for four or five months The process was said to have begun as a "small pimple" between the scapulas which the patient attributed to an insect bite received at the seashore At the time of the first visit, the patient presented a firm, reddish, indurated lesion measuring 4 fingerbreadths in diameter, between the scapulas The center was slightly raised and purplish, but gave no evidence of breakdown of tissue or fluctuation During a subsequent period of two weeks' observation, some exudation and a suggestion of superficial breakdown of skin were evidenced Three weekly injections of 300,000 units of penicillin in oil and wax were without effect on the process

The general physical examination disclosed nothing significant except a palpable liver edge 2 fingerbreadths below the costal margin There was no splenomegaly and no generalized or localized adenopathy The patient complained only of slight itching

The results of urinalysis were normal The serologic tests for syphilis elicited negative reactions A complete blood count revealed 79 per cent hemoglobin, 3,950,000 erythrocytes, 7,750 leukocytes, 58 per cent neutrophils, 3 per cent eosinophils, 34 per cent lymphocytes and 5 per cent monocytes, the color index was 1 01

Biopsy was reported to indicate lymphoblastoma and probable mycosis fungoides (The punch biopsy wound healed promptly)

The patient was given 600 r of roentgen rays in doses of 100 r over a period of sixteen days Exudation ceased after the second treatment, the induration regressed and the lesions flattened within two weeks

DISCUSSION

DR FRED D WEIDMAN When I first looked at the lesion, I thought that it might be Bowen's disease that had been overtreated The sections show that there is a reticuloendothelial disease, but I cannot quite make myself think that it is mycosis fungoides The epidermal changes are not sufficiently hyperplastic I think that it would come closer to being Spiegler-Fendt sarcoid, even though clinically that diagnosis would not quite fit But there are many of these reticuloendothelial disturbances that cannot be forced into some particular niche or pigeonhole that dermatologists have made Just as in Hodgkin's disease, there are atypical cases, and I think that this is one of them I cannot go further than to say that it is an abnormality of the reticuloendothelial system perhaps closer to Spiegler-Fendt sarcoid than to anything else

DR. MAX JESSNER, New York (by invitation) It is impossible to make a histologic diagnosis in the early stage of mycosis fungoides, since there is nothing characteristic histologically at that time Dr John Garb is treating patients with mycosis fungoides with antimony potassium tartrate U S P, and the results have been astonishing The patients react promptly to the therapy

DR J P SCULLY (by invitation) The diagnosis was made by exclusion I could think of no other lymphoblastoma that would produce no other systemic manifestations without other evidence of disease and persist for six months

Extensive Pityriasis Lichenoides et Varioliformis Acuta (Mucha-Habermann) Presented by DR REUBEN FRIEDMAN and (by invitation) DR HERBERT KAPLAN and DR JOHN B ROXBY JR

DISCUSSION

DR DONALD M PILLSBURY This is an unusually extensive and good example of this disease Whenever I see a patient with this disease, I am amazed that it can be so confidently classified in the textbooks in the parapsoriasis group There are many features of it which suggest a subacute infection, or at least a local reaction to the products of some infection I should like to hear Dr Blank discuss whether or not any such cases have been studied from the standpoint of a virus origin, I do not recall any such reports

DR HARVEY BLANK (by invitation) As far as I know, this particular disease has not been investigated recently along those lines At the moment, one of the means of investigation of such a case is to put the vesicle material directly on the little screens to be used in the electron microscope, and it is now possible within a matter of hours to differentiate smallpox from chickenpox Dr Geoffrey W Rake, of the Squibb Institute, has worked this out in considerable detail and is interested in material from any questionable case

DR. REUBEN FRIEDMAN Fluid from several of the vesicles was inoculated into the scratched cornea of a rabbit, with a negative reaction

DR LOUIS GOLDSTEIN Did this patient have lesions in the oral cavity in the acute stage?

DR REUBEN FRIEDMAN No Three days ago papular hemorrhagic lesions developed on the roof of the mouth and pigmented petechial lesions on the palms and soles

Multiple Recurrences of Infectious Syphilis Over Nineteen Years, Granuloma Inguinale Presented by DR HERMAN BEERMAN and (by invitation) DR MORTIMER S FALK

P D, a white man aged 40, presents pinkish verrucous-appearing hypertrophic growth on the ventral surface of the coronal sulcus, negative for Treponema pallidum on dark field examination The patient had primary dark field-positive syphilis in February 1928 He was treated with arsenical and bismuth preparations Dark field examinations were made on several occasions—December 1930, November 1932, April 1934 and November 1938, all with positive results (This case was first reported by Pariser [*J A M A* **113** 1206 (Sept 23) 1939]) The original lesion, however, did not heal completely at any time Granuloma inguinale was suspected as early as 1934 and a few injections of antimony potassium tartrate were

Résumé of Clinical Course

Date	Number of Injections	Drug	Serologic Reaction	Progress Note
2/29/28	. .	....	Kolmer 44 Kahn positive	Dark field-positive penile lesion
2/29/28-12/29/28	7	Arsphenamine Bismuth arsphenamine sulfonate	Kolmer negative	Patient lost from observation
9/19/30-9/25/30	2	Neoarsphenamine	Kolmer negative	Dark field-positive penile lesions
2/12/32 2/26/32	3	Bismuth subsalicylate	Kolmer negative	No clinical relapse
11/21/32	9	Trisodium arsphenamine sulfonate	Kolmer negative	Indurated, ulcerative penile lesion swarming with spirochetes, lesion was at same site as original monorecidive
1/19/33	9	Trisodium arsphenamine sulfonate, bismuth subsalicylate	Kolmer negative	
6/15/33 12/8/33	. 10	Trisodium arsphenamine sulfonate		Glans penis inflamed, ulcerative lesion
	10	Bismuth subsalicylate		
4/17/34 3/20/36	20	Trisodium arsphenamine sulfonate	Kolmer 00	Lesion on left side of glans penis, dark field-positive for T pallidum
	26	Bismuth subsalicylate	Kolmer 44 on 5 tests, 10/11/35 to 1/16/36	
8/13/34	3	Antimony potassium tartrate	Negative (cerebrospinal fluid) 1/24/36	On 6/19/34 inoculations (rabbit) were reported positive for T pallidum, lesion did not respond to therapy, possibility of granuloma inguinale considered
2/7/35	8	Fuadin®	Kolmer 44	Dark field-positive perianal condyloma and multiple indurated purulent secreting penile ulcers, condyloma healed under treatment
11/1/38	8	Arsphenamine	..... .	
8/1/39	3	Bismuth subsalicylate	Kolmer 44	
11/7/38	.	.. .		Ducrey test positive, Frei test negative
1/28/42 2/9/42	3	Bismuth subsalicylate	Kolmer positive	Patient returned with granulomatous lesion on frenulum which he stated had been present since original visit (14 years), dark field-negative for T pallidum, smear revealed presence of Donovan bodies
	3	Antimony potassium tartrate		
2/47	60	Penicillin, 2,400,000 units	Negative	Dark field-positive primary syphilis (diagnosed and treated in another institution)
10/2/47	.		Kolmer negative Kline negative	Patient returns with verrucous-appearing hypertrophic growth on ventral surface of coronal sulcus, dark field-negative for T pallidum
10/3/47	. . .			Biopsy granuloma inguinale

given In February 1947, dark field-positive primary syphilis was diagnosed at another institution, and the patient was given 2,400,000 units of penicillin According to the patient, the lesion did not heal

DISCUSSION

DR DONALD M PILLSBURY I did the original dark field examination on this patient in February 1928 As the history indicates, for many years thereafter, in spite of what was presumed to be good antisyphilitic treatment, lesions of early syphilis, from which T pallidum was recovered, continued to develop on his skin The patient apparently now has granuloma inguinale, but I would not doubt the capacity for infectious lesions of early syphilis to develop even now, in view of the past history A picture which I cannot get out of my mind in connection with this patient is that of rows on rows of filing cases in the Department of Medicine and Surgery of the Veterans Administration, all containing the records of men treated for syphilis in the Armed Forces Many of these have received penicillin therapy and, in the year 1945 at least, penicillin of very doubtful antisyphilitic potency When one observes relapses and/or reinfections after penicillin therapy and patients such as this one, the enormous potentialities of such patients in terms of the public health are very apparent Syphilis is far from being well controlled, and our methods to this end are still not so effective as they should be

DR DOUGLASS A DECKER, Allentown, Pa This is the first time that I have seen a white patient with granuloma inguinale

DR HERMAN BEERMAN I have seen this patient for nineteen years I can concur in the statement that he had a positive dark field examination in 1928 and that we obtained positive inoculation in rabbits with a portion of his penile lesion in 1934, even in 1934 we thought that he had granuloma inguinale, and he received some injections of antimony potassium tartrate then Every time that Dr Stokes wanted a dark field-positive lesion for teaching purposes he used to say "Get that boy" I think the primary diagnosis now is granuloma inguinale There were Donovan bodies present

FOLLOW-UP NOTE The patient was given 20 Gm of streptomycin intramuscularly in five days (Nov 25 to 30, 1947) The lesions healed promptly, without recurrence to date (October 1949)

A Case for Diagnosis (Senear-Usher Syndrome? Pemphigus Vulgaris?) Presented by DR CHARLOTTE JORDAN

DETROIT DERMATOLOGICAL SOCIETY

Henry A Brunsting, M D, *Chairman*

Hermann Pinkus, M D, *Recorder*

March 26, 1947

Necrobiosis Lipoidica Presented by DR H J PARKHURST, Toledo, Ohio

K D R, a married woman aged 39, presents on the inner aspect of the lower right shin a large coin-sized morphea-like patch of four years' duration, with sharp borders and some scaling of the surface The ivory-colored center shows telangiectases, and toward the border the tint was violaceous On the dorsum

of the left foot is a cluster of pea-sized brownish erythematous nodules grouped in a circle the size of a large coin These appeared after she had returned from Florida a week ago

Urinalysis and blood sugar studies showed no diabetes, and there was no family history of that disease

DISCUSSION

DR HARTHER KEIM The recent lesion on the left foot and the older one on the right foot look like granuloma annulare I wonder whether the large lesion on the shin is not the same

DR LOREN SHAFFER I agree with Dr Keim that this is a granulomatous process The older lesion is hardly typical of necrobiosis, because of the elevated border The youngest lesion has developed so quickly that it may be erythema diutinum Biopsy is indicated

DR ARTHUR JAMES The margin of the large lesion resembles granuloma annulare, the center looks like necrobiosis lipoidica

DR FELIX PINKUS The lesion looks like granuloma annulare, but everything on the legs below the knees is suggestive of necrobiosis

DR HARTHER KEIM We should keep in mind the case of Dr Belote's in which the disease later turned out to be ulcerating tuberculosis

DR HENRY BRUNSTING One must consider lipid disturbances of other types

DR HOWARD PARKHURST I am sorry that no biopsy could be done The lesion looked more typical when I saw the patient first, several months ago, and this is only the second time I have seen her The appearance of the patch has changed, possibly owing to the roentgen treatment she has received The lesions on the left foot are different, possibly due to insect bites, because she was in Florida, a week ago, when they suddenly appeared

Lupus Erythematosus Limited to the Lips and Buccal Mucosa in a Woman Aged 37, Duration Nine Years Presented by DR H J PARKHURST

Lupus Erythematosus of Mucous Membrane of the Lips and Buccal Mucosa in a Man Aged 37, Duration Eleven Years Presented by DR HENRY A BRUNSTING

Discoid Lupus Erythematosus of the Nose in a Woman Aged 41, Duration Fourteen Years Presented by DR HENRY A BRUNSTING

Two Cases of Congenital Ectodermal Defect (Incomplete) Presented by DR H J PARKHURST

Circumscribed Scleroderma Presented by DR ARTHUR JAMES

Circumscribed Scleroderma of Six Weeks' Duration (Scleredema?) Presented by DR ARTHUR JAMES

Multiple Idiopathic Hemorrhagic Sarcoma of Kaposi Presented by DR HENRY A BRUNSTING

J H, a Negro aged 61, first noticed small tumors on the soles of both feet about 1940 These have progressed to involve the entire right sole and toe and the left instep

Examination disclosed numerous pea-sized and larger round, firm nodules, pink to brownish, distributed over the soles and toes of both feet Some of the lesions, of a verrucous nature, have dropped out, leaving a pea-sized excavation

Results of laboratory examinations, including a complete blood cell count, differential count, urinalysis, serologic test for syphilis and roentgenogram of the chest, were all within normal limits A roentgenogram of the feet showed some disuse atrophy but no bone destruction A culture from the lesions of the feet disclosed gram-positive diplococci but no fungi Histologic examination disclosed a sarcomatous stage of multiple hemorrhagic pigmented sarcoma (Kaposi)

In addition to topical therapy, the patient received potassium iodide orally, and between Feb 11 and 19, 1947, he received seven roentgen treatments to the lateral surfaces of each foot (200 kilovolts, 50 cm distance, 4 mm of copper filter) for a total of 1,050 r to each area There was considerable improvement following radiation therapy

DISCUSSION

DR ARTHUR JAMES I saw this man seven years ago His feet were swollen and had draining sinuses Biopsy showed blastomycosis He improved very much with potassium iodide therapy

DR FELIX PINKUS Today I made a clinical diagnosis of Kaposi sarcoma, and the histologic picture seems to confirm this

DR HOWARD PARKHURST The lesions now look like the idiopathic sarcoma of Kaposi, but eight months ago the condition resembled mycetoma The sinuses which were present then cleared up with moist packs of potassium permanganate solution More recently, after roentgen treatment, the nodules have subsided

DR THOMAS MILLER I agree with the diagnosis of Kaposi sarcoma The most plausible explanation would seem to be that it has recently developed on the background of an older, infectious process

DR HENRY A BRUNSTING I believe that the clinical and histologic picture is consistent with the diagnosis of Kaposi sarcoma There has been considerable improvement in the clinical picture in the month since radiation therapy was administered

Porokeratosis (Mibelli) of the Thumb of a 7 Year Old Girl Presented by DR H J PARKHURST and DR HENRY A BRUNSTING

Bright Red Nodular Tertiary Syphilid on the Thigh, Duration Eight Years Presented by DR HENRY A BRUNSTING

News and Comment

GENERAL NEWS

Third Annual Clinical Session of the American Medical Association — The Third Annual Clinical Session of the American Medical Association will be held in Washington, D C, December 6 to 9

The Clinical Session will provide a full scale scientific program specifically designed for the general practitioner Outstanding physicians will discuss such subjects as diabetes, pediatrics, laboratory diagnosis, physical medicine and rehabilitation, arthritis, dermatology, diagnosis by means of the roentgen rays, cancer and poliomyelitis Coordinated with this outstanding scientific program will be approximately one hundred scientific exhibits which will present original work on the subjects discussed

The newest offerings of one hundred and twenty-five manufacturing firms will comprise the Technical Exhibition Here will be found the latest developments in scientific medical research, drugs and equipment

Televised surgical and clinical procedures, similar to those shown in color at the Annual Session of the American Medical Association in Atlantic City last June, will be presented at the Washington meeting The demonstrations will originate in the Johns Hopkins Hospital and will be shown on screens in the Armory The television schedule will be spread over four days

The House of Delegates will meet at the Hotel Statler during this session One of the first orders of business will be the annual selection of the general practitioner who has made an exceptional contribution of service to his community

An entertainment program for attending physicians and their wives is planned The highlight of this program will occur on Wednesday evening, December 7, when Philip Morris will originate its "This Is Your Life" broadcast from the Hotel Statler The radio program will be followed by a stage show, in which outstanding stars will participate

Blanks for hotel reservations and advance registrations may be found in *The Journal of the American Medical Association*

Book Reviews

Malattie cutanee e veneree ed alterazioni oculari By G Sala and P Noto, with prefaces by A Grosti and B Alajmo Pp 410 Palermo, Italy S F Flaccovio, 1948

This book, which is probably the most comprehensive monograph on the subject, is the combined work of the ophthalmologist, G Sala, and the dermatologist, P Noto, both of the University of Palermo, Italy The authors discuss, in parallel articles, the embryology of the skin and of the eye and all dermatoses and venereal diseases which may affect the eye and the lids The book contains a vast amount of factual, mostly clinical and often original, material in connection with a rather large bibliography

There are some shortcomings which should be corrected in a new edition There are no illustrations and no alphabetic index, and the paper is poor, probably because of postwar difficulties It would be to the advantage of the book if the authors would agree on more rigid editing It seems out of proportion to write a page or more on the dermatologic aspects of lichen planus and other dermatoses and then to mention, in a few lines, the rarity of participation of the eyelids The spelling of foreign names and titles of publications, especially in the German references, is poor Of greater importance than errors of this kind is the omission of discussion of the work of Brunsting and Sheard and others on the high threshold level of dark adaptation in pityriasis rubra pilaris However, these shortcomings should not distract from the great value of the work as a modern reference book

Of interest is the observation of the relative frequency of dermatogenous cataract in cases of generalized psoriasis In this connection, it may be mentioned that the authors estimate that cataract develops in 10 per cent of the patients with neurodermatitis (atopic dermatitis) This percentage appears to be a higher one than is observed in America, and the discussion should prompt a study of the eye in a large number of American cases

An Introduction to Dermatology By J H Percival, M D Eleventh edition Price, $9 Pp 349 Baltimore Williams and Wilkins Company, 1947

In general this is an excellent, small, yet complete book, in which the author well meets the difficult problem of attempting to cover a large and complex field briefly The material is well organized and clearly presented and indicates logical thinking throughout There are sufficient good colored illustrations to help the presentation greatly

Though brevity and a superficial approach are necessary in a book of this type, there seems to be an insufficient attempt made to link dermatology to the whole of medicine Mention of the more serious general involvement of the body of many dermatoses is omitted in the discussion of some conditions and but briefly touched on in others

American readers, although likely agreeing in general with the material presented, will undoubtedly have varying opinions regarding certain specific ideas expressed Among such controversial points, the following ones might be mentioned that the Senear-Usher syndrome is a type of generalized lupus erythematosus and that this syndrome is identical with pemphigus foliaceus, that dermatitis herpetiformis "may imperceptibly change its character to that of pemphigus," that twelve hours is sufficient time for patch testing and that "if there is no reaction, any suspicion of the substance used for the test may be dismissed"

Archives of Dermatology and Syphilology

VOLUME 60 NOVEMBER 1949—PART II NUMBER 5

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Society Transactions

ATLANTIC DERMATOLOGICAL CONFERENCE

David Bloom, M D, and Eugene F Traub, M D, *Chairmen*

Wilbert Sachs, M D, and George M Lewis, M D, *Secretaries*

Manhattan and New York Dermatological Societies

March 8, 1947

Cosmetic Repair (Surgical) of Lupus Erythematosus Hypertrophicus et Profundus. Presented by DR SAMUEL M PECK

E B, a housewife aged 40, is presented from Mount Sinai Hospital, New York, with an eruption which appeared after exposure to sun and which has been present since 1925 The patient has been under observation since 1926 She has received a great deal of therapy, including treatment with gold and bismuth preparations, cobra venom and other remedies, but finally improved with administration of suramin sodium (naphuride sodium®) Subcutaneous infiltrations appeared in 1938 With improvement, the infiltrations disappeared, leaving atrophic areas resulting in cosmetic defects

There are still a few areas of activity on the face and scalp consisting of circumscribed patches of atrophy and telangiectasia The sites of the defects have been filled in by means of skin grafts

The patient has been kept practically free of lesions by injections of naphuride® The dosage was 100 mg with increase at each injection until a maximum dosage of 300 mg was given All injections were intramuscular and given once a week From October 1945 until the present she has received several courses of this drug the first consisting of eleven injections and the second of eight The third course, which comprised seven injections, was begun in June 1946

The reason for presenting the case was the great loss of subcutaneous fat at the sites of the previous infiltrations, with scarring over the flush areas of the cheeks A repair, consisting of dermal grafts, was performed by Dr Michael L Lewin Only the dermal component of the graft was utilized in order to limit shrinkage as much as possible

DISCUSSION

DR FRANCIS P MCCARTHY, Boston May I ask Dr Peck whether, on the basis of its use in 40 cases, he feels that this drug is safe for use by the medical profession? It seems to me that it is a toxic drug, capable of producing a renal irritation, as evidenced by casts and albuminuria Personally, I would prefer to use a less dangerous remedy

DR MAURICE J COSTELLO I have used naphuride® in the treatment of lupus erythematosus in 6 cases, with spectacularly good results in 3 of them, in half of the patients severe toxic reactions developed and the use of the drug had to be discontinued One patient had disturbance of vision, 2 had swelling of the hands and feet accompanied with intense pruritus, others had pain and swelling of the

joints and in 1 the urine indicated renal irritation I believe that the drug is to be used with great caution It is effective, but it should be given only in the refractory, severe cases

DR. GEORGE C ANDREWS I agree with Dr Costello I think Dr Peck has had more experience with germanin in the treatment of lupus erythematosus than anybody in this city, and he can do things with it, perhaps, that the average physician cannot do I agree fully with his remarks, except that I think he should be a little more careful in explaining how toxic naphuride® is Severe anemia, hepatitis and nephritis occur from its use The total dose must be kept under 1 Gm for a long period I feel, as Dr Costello does, that it is an extremely toxic drug I no longer use it in cases of pemphigus, although I do use it for lupus erythematosus of the discoid type in small doses of 100 mg once a week for six or eight weeks If the patient is carefully watched, such doses are fairly safe In some cases fine results are obtained, and in others it does no good

A Case for Diagnosis (Lymphoblastoma? Pemphigus? Dermatitis Herpetiformis?) Presented by DR. ISADORE ROSEN

E A, a woman aged 70, had an eruption of four years' duration This began as vesicular plaques on the wrists and hands After roentgen ray treatment the eruption disappeared, but it soon recurred on the face, chest and extremities Since then there have been complete remissions and also exacerbations of varying degree, the patient having to be hospitalized on several occasions

The eruption during the past few years has been generalized and has consisted of grouped and fused lesions of vesicular character On the face and extremities infiltration has been frequently observed, and at times the lesions have been oozing or covered with scales At other times they have been annular, with central vesicular crusting, and have closely resembled pityriasis rosea In August 1946, shortly before her hospitalization, almost the entire surface of the skin was involved, except for the palms and soles At that time the patient presented on the face, neck and chest diffuse dull erythema, edema and exfoliation The rest of the body showed rounded erythematous lesions from 2 to 7 cm in diameter, with a scaly collar just inside the erythematous border In some areas there were flattened bullae containing clear fluid During the patient's stay in the hospital new bullae appeared from time to time

The Wassermann and Kahn reactions of the blood were negative Frequent blood counts showed leukocytosis, with a count which at times reached a figure of about 18,000, and a high eosinophil count, on some occasions as much as 27 per cent Roentgenograms of the lungs revealed moderate central thickening of the lymphomatous type, with clear peripheral lung fields A roentgenogram of the spine showed localized hypertrophic changes of the lower cervical area.

Patch tests with 30 per cent potassium iodide and potassium bromide ointment gave a strongly positive reaction Chemical studies of the blood, including determination of the nonprotein nitrogen, total protein, albumin, globulin, icterus index, calcium, inorganic phosphate and sugar, showed normal figures The last examination of the erythrocyte sedimentation rate during an exacerbation showed 93 mm per hour The basal metabolic rate was within normal limits

Four biopsies taken at different times were reported to show (1) chronic dermatitis, (2) neurodermatitic reaction, (3) psoriasiform dermatitis, and (4) pemphigus The description of the last slide was as follows "There is an

DR WILBERT SACHS This patient has had long-standing dermatosis, and a superimposed pemphigus developed I believe that the underlying dermatosis is a distinct dermatologic entity that has never before been described I have now seen about 6 such cases, and the microscopic picture is always the same There is a neurodermatitic reaction, with a focal cellular infiltration of plasma cells The process suggests an exudative discoid and lichenoid dermatosis on the one hand and a mycosis fungoides on the other Yet it is neither of these diseases but a definite entity falling somewhere between both Clinically these patients may have macules, papules, nodules or patches This patient also has pemphigus, probably due to a toxic reaction

DR WALTER F LEVER, Boston The cutaneous lesions are eczematous in nature It is possible that the disease will turn out to be mycosis fungoides Frequently in the prefungoid state of mycosis fungoides it is impossible to find in the histologic sections atypical cells which would establish the diagnosis of mycosis fungoides Instead, only banal inflammatory changes are present In regard to a diagnosis of pemphigus, I think that is a disease entity and does not develop as a toxic reaction secondary to another dermatosis I would not dare to make a diagnosis of pemphigus on histologic grounds alone, except in some cases of pemphigus vegetans Bullae may occur as an unspecific reaction, both in eczematous cutaneous disorders and in mycosis fungoides

DR WILBERT SACHS I did not intend to imply that this was a case of mycosis fungoides In fact, I believe that disease will never develop in the patient This is not the proper time to discuss the differentiation between dermatitis herpetiformis and pemphigus I am not convinced that we know what pemphigus is, to me, the lesions of that disease are toxic bullous manifestations There are certain characteristics on which a diagnosis of pemphigus can be made microscopically

DR GERALD F MACHACEK We have had similar problems at the Presbyterian Hospital in which the diagnosis was uncertain The lesions were pemphigoid or were thought to be those of Duhring's disease, and treatment with sulfapyridine was tried and found wanting One such case was presented before the New York Academy of Medicine last Tuesday Dr Vero found that the lesions in that case and in another disappeared with large doses of vitamin A Perhaps Dr Rosen has already tried that form of therapy

DR ISADORE ROSEN This patient has been under observation for more than four years The only subjective symptom has been intense itching, and her general physical condition has never been impaired I am of the opinion that this bullous eruption is probably due to the effects of treatment over many months

Poikiloderma Vasculare Atrophicans with the Histologic Picture of Mycosis Fungoides Presented by DR DAVID BLOOM

Dermatitis Factitia Dystrophy of the Nails and Keloids of the Palms and Soles Presented by DR GEORGE C ANDREWS

H C F, a widow aged 66 from the Roosevelt Hospital, has arteriosclerotic heart disease, diverticulosis of the colon and hypertrophic arthritis Her psychiatric status has not yet been determined

In 1935 the patient was told that she had a fungus infection of the finger nails, which she felt was the reason for her various functional and organic disturbances Since that time she has scraped her palms, soles and finger nails daily in order to "rid her system of disease"

There is almost complete absence of the finger nails and toe nails On the palms and soles are deep, red, linear, thickened areas On the hands, these extend over the palmar surfaces of the fingers

The Kline and Mazzini reactions of the blood are negative The urine is normal, and a complete blood count shows a moderate hypochromic anemia The basal metabolic rate is —4 per cent

Moniliasis Presented by Dr George C Andrews

R V, a girl aged 9, is presented from the Vanderbilt Clinic She was normal and healthy at birth and was well until the age of 2, when "double pneumonia" developed After this she remained underweight and had recurrent furunculosis which continued until the onset of the present illness In August 1943, when the patient was first seen, there was an eruption involving the scalp, mouth, nails and skin which had appeared ten months previously The patient had been hospitalized elsewhere, without improvement

On admission in 1943 the child appeared malnourished Purulent crusted lesions were present on the scalp The mucous membranes were covered with a grayish exudate, the nails were thickened, and many poorly limited, scaling, erythematous lesions were present on the shoulders

Extensive studies have been carried out in the three and one-half year period, only the pertinent findings are presented Repeated cultures of material from the scalp, skin, nails, mouth, sputum and feces were positive for Candida albicans Roentgenograms of the gastrointestinal tract in 1945 showed disturbed function of the ileum In 1946, agglutination of the blood serum for C albicans was positive in a dilution of 1 128

Examination of tissue from the back revealed intraepidermal pustules, with a leukocytic infiltrate in the pars papillaris of the corium

Locally, various preparations, including sulfur, sodium perborate, sodium propionate and gentian violet, have been used Crude liver extract multiple vitamin preparations, Candida vaccine and antiserum were used systemically In 1945, during a nine week period of hospitalization, a protoanemonin antibiotic was administered locally and orally Since July 1946 treatment has included iodine solution locally and strong solution of iodine with folic acid by mouth Recently there has been slight improvement in the cutaneous lesions, although the scalp, mucous membranes and nails are unchanged

DISCUSSION

Dr George C Andrews I have always believed in the use of iodine for moniliasis, and this case is presented to show the effect of that drug The patient has been helped a good deal She has also been getting folic acid by mouth during the past few weeks In the *British Journal of Dermatology* there have been reported cases of tropical sprue cured with folic acid

Dr Maurice Sullivan, Baltimore I should like to suggest to Dr Andrews, in case the eruption does not respond to iodine, the use of sodium caprylate, which has been reported to cure moniliasis when other fungicides fail

DR J GARDNER HOPKINS I would question Dr Peck's comments regarding Candida albicans on normal skin, because some years ago Dr Rhoda Benham made careful surveys of normal skin and found other species of Candida but could not find C albicans I think if the differentiation is properly made, one may say that M albicans is rare or nonexistent on normal skin It is found in the normal intestine I should like to testify to the improvement of this patient under Dr Andrews' treatment We had her under our care for some time, using sodium caprylate among other things, and she was much worse than she is today

DR DUDLEY C SMITH, Charlottesville, Va In Washington a symposium on antibiotics was held recently There were reports on two substances with fungicidal properties both on local application and on internal injection One was obtained from Bacillus subtilis, although it is not the same as subtilin, and is called "eumycin" The other was developed in the Department of Agriculture last year in an attempt to find something to counteract "tomato wilt" They obtained an extract from tomato leaves which is called "tomatin" Both agents, so the reports stated, have a good therapeutic effect in vitro in various types of fungus infections—monilia, trichophyton and yeast

DR C GUY LANE, Boston It seems to me that the disease moniliasis is increasing We seem to have had more patients in our clinic recently, and I am just as much impressed with the obstinacy of the disease as I was years ago I do not believe we have made much headway in therapy We have had 3 or 4 cases lately in which there was opportunity to make fairly careful studies, and we have run the gamut of therapy We have been interested in trying the method developed at Duke University, where a person with pulmonary moniliasis recovered after serum therapy (J A M A **130** 205 [Jan 26] 1946) I wonder if anything further has been done, perhaps in the way of increasing the titer of rabbit serum by gradually increasing doses A great deal more intensive study is needed in these cases because they are potentially serious Lesions involving the mouth and larynx are obstinate and become generalized, with a fatal ending

DR JASPER L CALLAWAY, Durham, N C We also have our troubles treating moniliasis of the skin at Duke Hospital The patient whom Dr Lane mentioned had pulmonary moniliasis and was treated with a stepped-up course of antiserum and eventually recovered We have not been able to cure any patients with generalized moniliasis of the skin, regardless of the type of treatment

Sarcoidosis (Leprosy?) Presented by DR MAURICE J COSTELLO

A Case for Diagnosis (Periarteritis Nodosa? Eosinophilic Granuloma?) Presented by DR FRANK C COMBES

This case was previously presented before the Section of Dermatology and Syphilology of the New York Academy of Medicine on Jan 7, 1947

Actinomycosis Presented by DR FRANK C COMBES

M A, a girl aged 17, is presented from Bellevue Hospital with a lesion of the left side of the mandible She was previously presented by Dr Maurice J

Costello at the New York Dermatological Society in January 1947 and by Dr Emanuel Muskatblit at the Section of Dermatology and Syphilology of the New York Academy of Medicine on Feb 4, 1947

DISCUSSION

DR. GEORGE M LEWIS At a recent meeting in Cleveland, Lamb, of Oklahoma City, discussed the therapy of actinomycosis and stated that it should include (1)

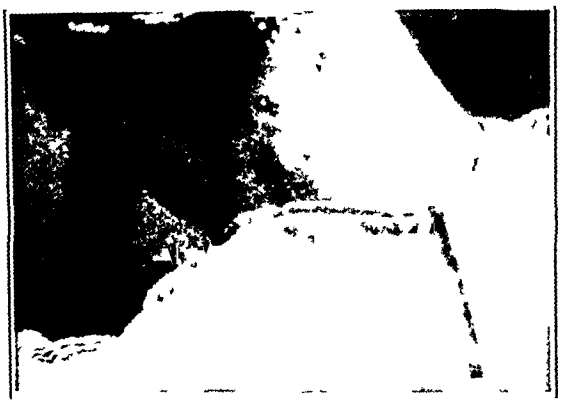


Fig 2—Periarteritis nodosa in a woman aged 35

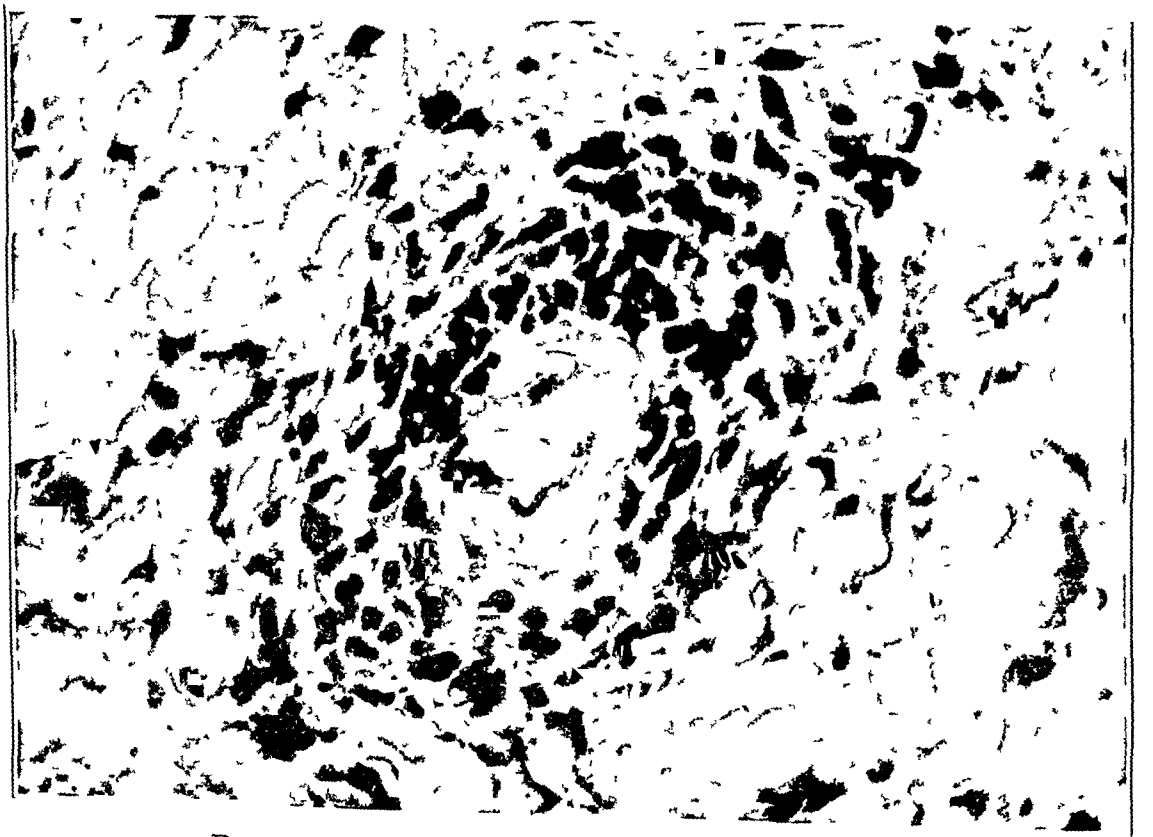


Fig 3—Photomicrograph of area of periarteritis nodosa

penicillin in large doses, which this patient has received, (2) one of the sulfonamide drugs, and (3) roentgen irradiation He favored this combination of remedies as superior to any one alone or to any other type of treatment now available

Dermatitis Factitia Actinomycosis? Presented by DR THOMAS N GRAHAM

Pachyonychia Congenita (Keratosis Palmaris et Plantaris Dystrophia Unguium and Leukoplakia Oris) Presented by DR FRED WISE

S H, a woman aged 40, and L H, her son aged 16, were previously presented before the Manhattan Dermatologic Society on January 14 by Dr Fred Wise

Both patients show hard, thick, painful, hyperkeratotic, lemon-colored growths on the soles, heels and toes The toe nails and finger nails are elongated, curved, discolored and dyskeratotic There are leukoplakic patches on the buccal mucosa



Fig 4—Dermatitis factitia in a woman of 38

and also on the tongue in the mother, who in addition presents dry, scaly, diffuse, seborrheic patches on the scalp Her basal metabolic rate was —20 per cent in February, and the son's was —14 per cent

DISCUSSION

DR FRED WISE This is the second case of the kind to be described in this country Cole and his collaborators described a case fully in the ARCHIVES, and this case is almost an exact replica of theirs The problem is one of therapy Both patients are practically crippled One lesion on the mother's knee was excised and a full thickness graft applied, and the growth recurred promptly in the area of the graft Dr Peck suggested administration of large doses of vitamin A, and this is being given, but too little time has passed to expect results I am pessimistic about any treatment whatever, except possibly an orthopedic procedure to permit the patient to walk with some degree of comfort



Fig 5—Hyperkeratotic growths of pachyonychia congenita in a boy aged 16



Fig 6—Dyskeratotic toe nails and finger nails in same boy as in figure 5

Incontinentia Pigmenti Presented by DR J GARDNER HOPKINS

J A M, a girl aged 5½ months from the Vanderbilt Clinic, was previously presented by Dr Helen O Curth before the Section of Dermatology and Syphilology of the New York Academy of Medicine on March 4, 1947

Most noticeable on the inner aspect of the thighs but visible also on the sides of the trunk are wavy parallel bands of hyperpigmentation in typical zebra pattern The skin is otherwise normal

DISCUSSION

DR FRED WEIDMAN, Philadelphia A number of years ago I performed an autopsy on an infant with peculiar transverse bands of pigment across the abdomen, but in paraffin sections I could not find the pigment which was to be expected Perhaps Dr Hopkins has had the same experience, because in his sections the pigment was inconspicuous However, in frozen sections, it was conspicuous indeed It is true that melanin pigment is not supposed to be dissolved in our histologic embedding agents, but perhaps in Dr Hopkin's case, too, frozen sections would show the pigment more plainly than do the histologic sections I reported my case under the name of "Transverse Hyperpigmented Lines of the Thorax and Abdomen of a Negro Infant" in the ARCHIVES (**37** 517-523 [Aug] 1919)

DR J GARDNER HOPKINS Was the pigment in the epidermis or in the chromatophores?

DR FRED WEIDMAN, Philadelphia In the epidermis

DR GERALD F MACHACEK This type of disorder has also been reported as familial chromatophore nevus by Naegeli and as melanodermatosis congenita by Siemans

DR J GARDNER HOPKINS I do not believe that this case is parallel to Dr Weidman's It corresponds to the cases described by Naegeli and by Bloch and Sulzberger in which pigment was in the chromatophores under the skin and not in the epidermis

A Case for Diagnosis (Behcet's Syndrome? Pemphigus? Leukemia Cutis?) Presented by DR EUGENE F TRAUB

A Case for Diagnosis (Lichen Planus and/or Lupus Erythematosus of Lips and Tongue Oriental Sore of Forearm) Presented by DR MAURICE J COSTELLO

G R, presented from Bellevue Hospital, was born in the United States and was taken to Greece when he was 14 years old, where he remained until about four months ago He was a guerilla fighter during the past two years in Greece. He does not smoke

About 15 months ago an erythematous patch appeared on the patient's right forearm, persisting until about three months ago, when it developed into an ulcer After biopsy was performed at this site the ulcer healed spontaneously A hyperpigmented scar can be seen

About four months ago a small superficial red area appeared on the left side of the dorsum of the tongue It increased in size to that of a 25 cent piece, became superficially eroded with a grayish pellicle-like border, and caused some pain when the patient was eating and drinking

During the past three weeks reticulated whitish streaks on the lower lip suggestive of lichen planus have developed A small superficial erosion has recently developed on the center of the tongue, medial to the one just described There has been no regional adenopathy

Dark field examinations of the lesions on the tongue and arm gave negative results, as did the Mazzini reaction of the blood A complete blood count, examination of the urine and roentgenograms of the lungs revealed no abnormalities

Biopsy of the lesion on the arm, done at Bellevue Hospital, showed a nonspecific granuloma with epithelioid cells, plasma cells and lymphocytes

Material from the lesion on the left side of the dorsum of the tongue was examined by Dr Fred D Weidman, who reported the lesion to be syphilis or oriental sore He found the epidermis to be enormously acanthotic and parakeratotic Although its squamous cells were greatly swollen, there was no evidence of neoplastic activity, even at the basement membrane There the basal cells had undergone metaplasia into squamous forms There, too, many of the inflammatory infiltrative cells of the corium were infiltrating the epidermis A rather heavy infiltration of inflammatory round cells lay immediately below the epidermis It crowded the papillae but did not extend farther than the subpapillary plexus of vessels The cells were distributed diffusely, and although lymphocytes were dominant, there was a large intermixture of elongated nuclei which were interpreted as epithelioids However, none of them was congregated into individual foci in such a way as to constitute miliary granulomas There were numerous other elongated nuclei which were clearly those of histiocytes, but they were readily distinguishable from the plumper epithelioid ones

The significant features in the diagnosis resided in the epithelioid cells Such cells do appear in the lesions of oriental sore, but in the absence of the specific organisms the epithelioids could reasonably be those of syphilis or tuberculosis, the diffuse distribution would point more toward syphilis The protozoa were not recognizable in these sections

DISCUSSION

Dr Fred Weidman, Philadelphia The solitary item of significance in the histologic picture is the presence of epithelioid cells, which are not gathered into foci to indicate definite miliary granulomas of either syphilis or tuberculosis In other words, it is a diffuse reaction such as occurs in pneumonia alba In such a situation it is necessary to resort to methods for the identification of the parasite itself I might say that the only time recently that I have seen the Leishman-Donovan body in sections was at Dr Lloyd W Ketron's laboratory, but that is unusual A much more preferable method of demonstrating the parasites is by means of smears, so I should say that if the pursuit of the Leishman-Donovan body is to be continued, that is the method of choice After seeing the patient today, I do not think the lesion could be that of leishmaniasis, as the infiltration of the tongue is not particularly heavy It is rather superficial for that disease, and leishmaniasis is usually more suppurative, as I recall it, there is no evidence of pus in the sections After seeing the patient again, I do not think it is likely to be syphilis, which I intimated in the histologic reports I was swayed by the fact that the infiltration is diffuse

Dr Clarence S Livingood, Philadelphia Several years ago I had an opportunity to observe a rather large number of patients with cutaneous leishmaniasis, and this case certainly does not correspond with any of those which I have seen I gathered that the type of ulcer which the patient had was not characteristic of that disease According to the information which I obtained from him, his stay abroad was entirely confined to Greece, and as far as I know leishmaniasis does not occur in that country

Dr Bernard Appel, Lynn, Mass The lesions on the lips and in the mouth are, in my opinion, consistent with lupus erythematosus It is not unusual, in my experience, to find lesions on the lips which in the early stages resemble those of

lichen planus clinically because of the white reticulation and their limitation to the vermillion of the lip With the progress of the disease, however, the lesions become more characteristic as they extend to the glabrous skin I anticipate that that is what will happen in this case Furthermore, I have not found that lichen planus produces such extensive and persistent ulceration of the tongue when it does occur there, that is to say, this picture is more consistent with lupus erythematosus If it actually is lupus erythematosus, it is also my opinion that it is likely to be extremely resistant to treatment and that the prognosis should be guarded

DR FRANCIS P MCCARTHY, Boston Dr Weidman, does the lesion on the tongue show epithelioid tissue?

DR FRED WEIDMAN, Philadelphia Yes

DR FRANCIS P MCCARTHY Do we get this reaction in lupus erythematosus?

DR FRED WEIDMAN No

DR MAURICE J COSTELLO The question of tuberculosis of the tongue also came up, but roentgenograms showed the chest to be normal We have seen patients who had both lichen planus and lupus erythematosus simultaneously I think the lesions on the lower lip suggest lichen planus and am inclined to agree that the lesion on the tongue is lupus erythematosus or lichen planus clinically

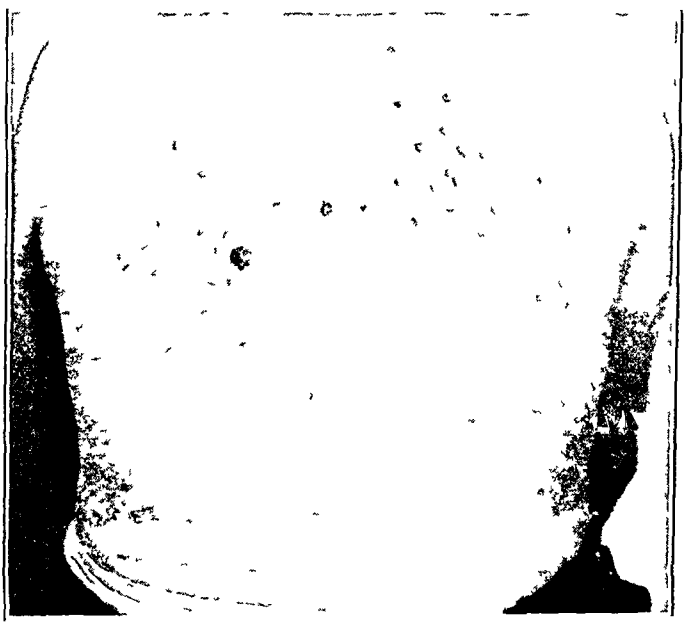


Fig 7—Lesions of leiomyoma

Leiomyoma Presented by DR ANTHONY C CIPOLLARO

P P, a man aged 52, is presented from the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, with an eruption of fifteen years' duration which has not changed essentially in the past twelve years

In the scapular region there is a symmetric eruption of slightly reddish, mostly oval, elongated and spherical infiltrated, firm, nodular lesions which are arranged in the lines of cleavage There is a moderate number of similar but smaller and less indurated lesions in the lower lumbar and gluteal region Some of the lesions are tender to pressure The patient complains of severe pain in the region of the eruption during cold weather



Fig 8—Photomicrograph showing leiomyomatous changes

Routine examination of the blood and urine gave normal results

Biopsy of a nodular lesion was reported previously to show neuroma Recently another biopsy was reported as showing leiomyoma

Unfiltered roentgen irradiation seems to have alleviated the pain of which the patient has complained

DISCUSSION

DR WILBERT SACHS I made both diagnoses I feel that in regard to multiple small lesions for which the diagnoses of both neuroma and leiomyoma are suggested it is possible that it is not a single, distinct type of tumor but a combination of both Of course it is often difficult to differentiate between neuroma and leiomyoma In this case we did some special stains on the first section and these showed a neuroma On the second section it was not necessary to do any special stains since there was a classic picture of leiomyoma

Pityriasis Rubra Pilaris Uninfluenced by Treatment with Vitamin A Presented by DR E W ABRAMOWITZ

Ragweed Dermatitis Presented by DR MAX SCHEER

P B, a man aged 65, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital He loads Pepsi-Cola bottles as an occupation He was in good health and free from any cutaneous disease until September 1936, when he walked through some lots in Astoria, N Y, without stockings A vesicular eruption appeared on the dorsa of the feet and legs which was at first called eruption from poison ivy and which lasted five months It recurred in September 1937, when it was slight on the feet and legs, mild on the face, hands and forearms and severe on the scrotum The eruption then became perennial, with exacerbations from September to May June and July are the most comfortable months for the patient

There is a thickened, lichenified eruption on the face and forearms The eruption stops rather abruptly on the upper third of his forehead, which is protected by his hat

Reactions to patch tests with oleoresins of short ragweed, cocklebur, sheep sorrel, Kentucky blue grass, red top, poison ivy, orchard grass and timothy were positive Patch tests with the protein extracts of trees, grasses and weeds showed a positive reaction only to oak Scratch tests with these protein extracts gave negative results

The histologic picture was that of a contact type of eczema

No specific treatment has been given as yet The patient has been receiving eight 50 mg tablets of tripelennamine hydrochloride (pyribenzamine®) daily, with only slight alleviation of the itching

DISCUSSION

DR JOSEPH MULLER, Worcester, Mass From the appearance I would be likely to believe that it is a ragweed dermatitis, but, on looking at the calendar and the patient, I just cannot accept that diagnosis After all, ragweed dermatitis is nothing else but a contact dermatitis, and the patient has certainly not been exposed to ragweed for a long time The fact that the reactions to patch tests were positive means nothing I think the patient has at some time had contact dermatitis If ragweed caused the trouble, it should have started in the fall and be over by now

DR JOSEPH GOODMAN, Framingham, Mass In cases of ragweed dermatitis, which lasts around the year, it must be remembered that there is often a cross sensitization between ragweed and Pyrethrum I note that other tests were done in this case, but I see no reference to Pyrethrum It would be possible for the patient to be exposed to Pyrethrum the year round That should be considered as a possibility

DR BERNARD APPEL, Lynn, Mass I should like to confirm the observations made by the last speaker and also to point out the fact that many patients subject to ragweed dermatitis are those who live in the country and work around barns where sprays against flies and insects are used, and of course we know that they contain Pyrethrum and products of that family In my opinion it is important to do patch testing with these substances, as well as with the solvents used in insecticides

DR DONALD S MITCHELL, Montreal This man has never been hospitalized I wonder whether it would help to admit him and remove ordinary contacts such as clothing and soaps

DR JACK WOLF The eruption on the torso as seen today is incidental, it developed after a recent cold and may be the result of medication which he received It has no relation to the other eruption This man has been tested with other oleoresins as well as ragweed fractions We have had a number of cases of ragweed dermatitis in which persistent eruptions developed and remained throughout the entire year after several seasonal attacks This persistence may be due to the development of sensitization to other allergens which act at the same site

Lymphoblastoma Mycosis Fungoides with Eczematous Lichenoid and Granulomatous Lesions Presented by DR A BENSON CANNON

OTHER CASES PRESENTED

A Case for Diagnosis (Dermatitis Medicamentosa? Senear-Usher Pemphigus? Dermatitis Herpetiformis?) Presented by DR JACK WOLF

Purpura Hemorrhagica Presented by DR EUGENE F TRAUB

Tuberculosis Cutis Colliquativa Improved by Calciferol Therapy Presented by DR NATHAN SOBEL

A Case for Diagnosis (Macular Atrophy? Lichen Planus Atrophicus?). Presented by DR JACK WOLF

Parapsoriasis Guttata Presented by DR MAX SCHEER

A Case for Diagnosis (Lymphoblastoma? Mycosis Fungoides?). Presented by DR FRED WISE

Dyskeratosis Congenita with Pigmentation, Dystrophia Unguium and Leukoplakia Oris. Presented by DR FRED WISE

Circinate Sarcoid Presented by DR EUGENE F TRAUB

A Case for Diagnosis (Erythroderma Ichthyosiforme Congenitum? Erythroderma Exfoliative Universalis Tuberculosa?) Presented by DR A BENSON CANNON

BROOKLYN DERMATOLOGICAL SOCIETY

Abraham Walzer, M D, *President*

Seymour H Silvers, M D, *Secretary*

March 17, 1947

Mycosis Fungoides in a Patient with Psoriasis Presented by Dr L M Waterhouse

J J, a man aged 46, born in the United States, first consulted me twelve years ago, at which time a diagnosis of psoriasis was made Six or seven years ago he was treated at a well known New York dermatologic clinic where the diagnosis was confirmed clinically and histologically He had received ultraviolet rays, coal tar preparations and other topical medication There was no history of his ever having received arsenic preparations Two years ago the lesions became raised and tumor like At that time a biopsy specimen from one of these lesions was reported as suggesting lymphoblastoma, but no more definite diagnosis was made The biopsy was repeated two months ago by another histopathologist, who suggested the possible diagnosis of mycosis fungoides

Results of repeated serologic tests for syphilis were negative Results of blood cell counts and urinalyses were normal

Examination shows a generalized eruption There are quarter-sized to dollar-sized flat, red, scaly patches There are a few lesions on the lower part of the back and thighs, which are raised and tumor like The face shows an ill defined erythema with scaling On the scalp are similar patches with alopecia

DISCUSSION

Dr Seymour H Silvers This is a most unusual case It seems that the diagnosis of psoriasis was established independently by different competent dermatologists This diagnosis was corroborated by histologic studies At present there are seen a sufficient number of lesions which are infiltrated and tumor-like to warrant a clinical diagnosis of granuloma fungoides However, we cannot completely ignore the findings of two able histopathologists who failed to corroborate the diagnosis of granuloma fungoides It is not unusual for the histopathologist to fail the clinician when the latter needs him most

Dr L M Fruchtbaum The picture is not that of psoriasis On the other hand, there are two large lesions and numerous smaller ones on the body and extremities which are definitely infiltrated In spite of the fact that the patient feels and looks physically well, I believe that this is a case of mycosis fungoides

Dr E A Gauvain I believe that the disease in this case was originally mycosis fungoides, as it is now I did not see any lesions typical of psoriasis on this patient, although such a diagnosis might have been considered in a few lesions had they been the only ones present I have never seen a case of undisputed psoriasis, even though followed through many recurrences, that terminated as mycosis fungoides Clinically there is now a polymorphous type of lesion, changing in character, of a dusky color, causing some itching and finally developing into nodules, which, to my mind, are typically mycosis fungoides

Dr Abraham Walzer Clinically, this is a case of mycosis fungoides The disease developed in a manner that it does in many cases It never was psoriasis, irrespective of the fact that histologically it was first reported as psoriasis

Mycosis fungoides may begin with what may appear to be psoriasis, parapsoriasis, eczema or any other condition I believe that just as the clinical picture, at the start, may be atypical, so the histologic picture may be more or less vague and indefinite At the present, this man shows lesions which, to my mind, are classic examples of mycosis fungoides

Epithelioma of Penis Presented by DR S I GREENBERG

Multiple Keloids Presented by DR MAX LERNER

J G, a girl aged 12, was seen at the Kings County Hospital Dermatologic Clinic on March 3, 1947 She had chickenpox in October 1946, and "marks" developed where there had been blisters

There are hard nodules, pea to bean size, distributed on the face, neck, abdomen and thighs Some are colorless and others yellowish white A few are erythematous with telangiectasia All the lesions are limited to the sites of the original varicella blisters There is no history of keloidal scars from previous injuries

DISCUSSION

DR ABRAHAM WALZER The keloid tendency does not have to be present during the entire life of the patient There may be periods when the tendency does not show itself My experience has been that if keloid is treated before it has been present six months, with roentgen rays, there is a chance of flattening of the lesion After six months, roentgen therapy is of no value This has been explained on the principle that connective tissue cells mature in about six months When the cell becomes fully mature, it cannot be reduced, but as it is growing and developing (that is, up to six months), its growth can be stopped No matter how much roentgen therapy is given after six months, it is of no value However, if the lesion is excised and roentgen rays given, the lesion may be suppressed

Generalized Sarcoidosis Presented by DR MAX LERNER and DR FRANK D JENNINGS JR (by invitation)

Abraham Walzer, M D, *President*

Seymour H Silvers, M D, *Secretary*

April 21, 1947

Xanthoma Tuberosum Presented by DR C T CHIARAMONTE

Xanthomatosis Juvenilis Presented by DR C T CHIARAMONTE

V S, a white girl, aged 5 years, has several discrete, bean-sized, yellowish nodules on the face and neck Her liver is enlarged to 2 fingerbreadths below the costal margin with an even, smooth edge

This child was first seen when she was 6 weeks old She showed many shiny, yellowish nodules which were generalized and of varying sizes There was a reddish halo around the lesions Some of the larger ones were oval in shape Many of the lesions showed multiple punctate depressions at the follicular orifices Lesions were also found on the mucous membranes of the mouth The lesions were noticed soon after birth

The infant was placed on a low fat diet and was reexamined a year later It was observed that occasionally there was a generalized flushing of the skin During the period of observation, some of the lesions appeared vesicular, the mouth lesions disappeared and the cutaneous nodules grew in size Many of the lesions showed flattening at the periphery, and a few lesions disappeared Since then all lesions have undergone involution except those on the face and neck The skin at the sites of former lesions has become brownish red There has at no time been any jaundice or pigmentary changes affecting the normal skin

A biopsy performed during infancy revealed a dense infiltrate in the cutis, consisting of epithelioid cells, the cytoplasm of which had a vacuolated appearance and simulated fat cells

DISCUSSION

DR SEYMOUR H SILVERS I followed 2 cases of xanthomatosis juvenilis for many years The patients came under my care during the first month of their lives I watched new lesions appear, and, as the children became older, the lesions gradually flattened out and finally disappeared I believe that, regardless of therapy, the lesions of xanthoma juvenilis will disappear when the child reaches the age of 6 to 7 years It is likely that xanthomatosis juvenilis should be classified with the nevi rather than with the diseases due to metabolic disturbances

DR ABRAHAM WALZER These patients should have a complete determination of the lipids of the blood Increased cholesterol does not necessarily imply that every case of xanthomatosis is due to cholesterol disturbance If any other fats are disturbed, the cholesterol may be increased in the blood To what is the yellowness of the cholesterol lesions due? Cholesterol and its esters are white, but the lesions are not The yellowness is probably due to a lipofuscin substance found in the fat

Tuberculosis Cutis with Papulonecrotic Sarcoid-Like and Colliquative Lesions Presented by DR S B FRISCHBERG

Alopecia Congenita Presented by DR C T CHIARAMONTE

D B, a white girl aged 9 years, has scant growth of hair on the scalp and eyebrows The deficiency is more evident in the frontal region There is pronounced follicular keratosis on the nape of the neck The child weighed 6 pounds, 2 ounces (2,778 Gm) at birth, was a breech presentation at delivery and gained weight more slowly than the average infant Since birth the hair on the scalp had always been sparse

The laboratory examination revealed absence of arsenic in the urine, a basal metabolism of + 13 per cent and a normal reaction for specific dynamic action of proteins A roentgengram of the sella turcica was normal

DISCUSSION

DR SEYMOUR H SILVERS Often, in addition to absence of or sparse hair, other ectodermal defects are seen It is not unusual to observe alopecia with dental and ophthalmic defects This child is mentally alert and bright.

DR JOEL SCHWEIG I am in favor of the diagnosis of the presenter, but I would advise cultures be made from the scalp and hair as the picture may turn out to be one of favus

Epidermolysis Bullosa Congenita Presented by DR C T CHIARAMONTE

G O, a white boy aged 4 years, has numerous bullae on the dorsum of the feet, some of which are hemorrhagic The toe nails and finger nails show atrophic and dystrophic changes Healed, erythematous lesions may be seen on the elbows and knees

There is no consanguinity of the parents It is interesting to note that this child has a nonidentical twin brother who is normal This child was first observed a few days after birth At that time, there were numerous cloudy bullous lesions scattered on the body, which I diagnosed as pemphigus neonatorum Culture from the bullae revealed the presence of Staphylococcus albus The lesions disappeared after treatment with sulfonamide drugs locally and internally Since then, however, blisters have been noticed by the parents to be reappearing on the extensor surfaces of the elbows and knees, on the dorsa of the feet and in the mouth

A Case for Diagnosis (Hodgkin's Disease?) Presented by DR C T CHIARAMONTE

L A, a white man aged 43 years, has a generalized, itchy eruption consisting of isolated, large, serrated papules These papules are brownish red, and some of them are excoriated There are also irregular groups of large vesicles, the tops of many present a small yellowish crust located on the extensor surfaces of both legs, arms and forearms and on the dorsa of the hands On the thighs the lesions have spread peripherally and form patches of crusted vesicles Groups of vesicles are present on the face, chest and abdomen Several of the original lesions have left a brownish pigmentation

The patient has had papular lesions and itching for the past seven months He first presented himself for treatment in January 1947, after having been treated elsewhere for scabies The past history reveals that the patient has had pulmonary tuberculosis, which was recognized in 1928 and was pronounced arrested in 1935, after a phrenicectomy In 1943 he received treatment for spastic colitis

A recent roentgenogram of the chest and examination of the gastric contents for tubercle bacilli did not reveal any abnormalities A biopsy of one of the papules performed in March revealed moderate acanthosis and parakeratosis with some hyperkeratosis The epidermis was infiltrated with eosinophils The corium contained many eosinophils, round cells and proliferating fibroblasts This inflammatory infiltrate was grouped around the small blood vessels The results of the urinalysis and hemogram were within normal limits The cholesterol content of the blood was 197 8 mg per hundred cubic centimeters and the cholesterol esters were 67 9 mg Roentgenograms of the long bones showed no abnormalities

DISCUSSION

DR C T CHIARAMONTE The biopsy was performed on one of the nodular purplish brown, persistent lesions I have known of cases of early Hodgkin's disease which was mistaken for scabies The patchy eruption on the arms, forearms and legs has appeared only in the past two months I shall observe him closely In the past few months, there has been a rise in the white blood cell count

DR NATHAN PENSKY The suggestion of Dr Chiaramonte must be seriously considered Several articles in the current literature have appeared on eosinophilic granuloma However, I have seen a number of patients who have been overtreated for scabies in which an eczematized eruption developed which clinically resembled

the rash in the case presented tonight The histologic observations in the present case would lead one to suspect the possibility of a lymphoblastoma

DR C T CHIARAMONTE Another thing of interest is the tuberculous background I feel that Hodgkin's disease and tuberculosis are in some way related

DR JOEL SCHWEIG I have the feeling that the diagnosis of Duhring's disease is the right one, as I have seen several instances of that condition which resemble clinically the case presented tonight My suggestion is that the patients be tested with potassium iodide, internally and externally, and that he be treated with sulfapyridine

Mycosis Fungoides, Developing On Parapsoriasis(?) Presented by DR C T CHIARAMONTE

Abraham Walzer, M D, *President*

Seymour H Silvers, M D, *Secretary*

May 19, 1947

Generalized Scleroderma Presented by DR L M FRUCHTBAUM

A M, a woman aged 70, was admitted to the Unity Hospital on Jan 6, 1947, because of acute cardiac decompensation Examination revealed edema of the lungs and of the legs The patient gave a history of progressive dysphasia for the previous three years, during which time she had noticed thickening and hardening of the skin of the forehead and face with inability to open the mouth wide The patient also noticed that she was unable to smile or frown and experienced difficulty in swallowing foods, particularly hard foods The hardening of the skin extended to the neck, shoulders, chest, back and thighs Examination revealed a waxy smooth skin adherent to the underlying soft tissues on the face, neck, trunk, shoulders and thighs The fingers and toes were not affected

The hemogram was within normal limits except for a leukocyte count of 12,500 per cubic centimeter Blood chemistry studies gave normal values for sugar and cholesterol, but the urea nitrogen was elevated to 28 5 mg per hundred cubic centimeters, and creatinine to 2 mg per hundred cubic centimeters The basal metabolic rate was —36 per cent The urine was normal Histologic examination of a specimen of skin showed scleroderma

DISCUSSION

DR JOEL SCHWEIG In view of the fact that there is so much edema present on the neck, as well as the lower extremities, I feel that the process is a deep-seated one and may be scleredema of the infectious type as described by Buschke Should it be of infectious origin, treatment with penicillin or sulfonamide drugs would be indicated and the prognosis would be more favorable A biopsy should aid in the final diagnosis

DR JACOB SKEER I also believe that there is too much edema present and that the extension of the lesion was rather rapid By this time there should be contracture of the tissues and other signs, like pigmentation The edema is of the nonpitting type and suggests Buschke's disease I think that a biopsy would give more information

DR SAMUEL I GREENBERG I think that this is scleroderma Scleredema is described in young adults, it follows infectious disease and is transient These aspects are not present in this case

DR DAVID M DAVIDSON I think that this is scleroderma The patient also has cardiac disease, and the pitting of the legs has nothing to do with her scleroderma I do not believe that this is scleredema of Buschke because the duration of the condition is three years and there is no history of a preceding infection

Urticaria Pigmentosa Presented by DR L M FRUCHTBAUM

DISCUSSION

DR C B LOCASTO It has been found that in animals given a diet free of vitamin A large numbers of mast cells develop in the tissues of the body In view of this, it is suggested that the patient receive large doses of vitamin A

Case for Diagnosis (Granuloma Annulare?). Presented by DR L M FRUCHTBAUM

Case for Diagnosis (Necrobiosis Lipoidica Diabeticorum? Granuloma Annulare?) Presented by DR I N HOLTZMAN

The patient, a white housewife aged 51, was first seen in the outpatient department of the Jewish Hospital of Brooklyn on May 12, 1947, with the following history

About five weeks prior to admission, she first noticed a nonitching eruption on both forearms and eyelids, which followed a mild abrasion of the left forearm The eruption has remained unchanged since its onset Her past history revealed the existence of diabetes mellitus of at least ten years' duration and a mild hemostatic eczema of the right ankle of about seven years' duration

Examination on admission revealed a papular eruption on the volar aspect of both forearms and eyelids The lesions varied in size from that of a pinhead to that of a pea and were faintly erythematous, and the larger papules were slightly yellow There was no characteristic grouping or configuration of any of the lesions

A biopsy of a lesion of the left forearm showed degeneration, necrobiosis and homogenization of the collagen with nuclear debris Surrounding and infiltrating into this zone were large collections of epithelioid foam cells Small round cells were occasionally seen Blood chemistry studies revealed a concentration of sugar of 181 mg and cholesterol of 261 mg per hundred cubic centimeters

DISCUSSION

DR JOEL SCHWEIG In my opinion the clinical features of the case fit in well with the diagnosis of lichen ruber moniliformis, which was well reviewed by Wise and Rein in 1936 The shape of the lesions, the color and the distribution are typical Although there is only one area on the right wrist presenting the moniliform features, it should be considered lichen ruber moniliformis, as those features may appear later in abundance The histologic observations are also like the microscopic features of lichen ruber moniliformis

DR DAVID M DAVIDSON When the patient was first seen at the clinic, a few diagnoses were mentioned, among them lichen moniliformis and lichenoid sarcoid When I examined the slide and saw that the main histologic changes

"The roof of the mouth is beefsteak red, and beefy and has a white exudate on it There are deep furrows The same picture is present on the sides of the cheeks and on the uvula The pharynx is red and 'angry looking' There is one small lesion on the gum over the left upper incisor"

An oral surgeon called in consultation stated The patient appears to have an inflammatory hyperplasia of the oral mucosa, very marked on the palate, with fissures I saw the patient at the suggestion of Dr John G Downing, who had seen the previous patient (case 2) at a meeting of the New England Dermatological Society and suggested that this patient probably had pyostomatitis vegetans The following is my consultation note

"Examination of the oral cavity shows a soft verrucous eruption of the hard and soft palate mucosa extending downward to include the uvula The mucosa of both cheeks shows folding in the molar regions but no active process at the present time Minute pinpoint whitish abscesses can be demonstrated in the lesions of the soft palate and uvula There are a few miliary abscesses in the upper part of the vestibule of the mouth in the cuspid regions The tongue shows an area of denudation of the coating, probably due to contact irritation from lesion of the palate The picture is strongly suggestive of a condition known as pyostomatitis vegetans"

Following is the report on the biopsy specimen taken from the palatal region of an old verrucous lesion

"The epithelial surface shows moderate hyperkeratosis and marked acanthosis with broadening of the rete pegs The underlying tunica propria shows a marked dense cellular infiltration with disorganization of the collagen fibers There is moderately increased capillary vascularization The cellular infiltration is very pronounced in the subepithelial zone and the papillas and extends into the epithelial surface forming dense collections of cells made up principally of lymphoid and plasma cells There is spongiosis of the acanthotic epithelium with many infiltrating lymphocytes extending to the surface epithelial layer The cellular infiltrate in the tunica propria is pleomorphic, with plasma cells predominating and relatively few polymorphonuclear leukocytes An occasional multinucleated cell is seen, and only a rare eosinophil is demonstrated The picture is that of a granulomatous inflammatory process of a chronic type The relative absence of eosinophils in this case as compared to the marked eosinophilia seen in early lesions can be explained by the age of the lesions The clinical picture together with the histologic findings indicates a chronic granulomatous process involving the oral cavity Two other cases of pyostomatitis previously seen by me differ only in that in more acute lesions the eosinophils predominate in the cellular exudate The diagnosis is pyostomatitis vegetans"

A report from the family physician received in November 1948 stated that there had been an improvement in the oral condition a year ago but that he had not seen the patient since that time

CLINICAL DESCRIPTION AND COURSE OF ORAL LESIONS

There was a remarkable similarity in the clinical courses in all 3 cases In cases 1 and 3 the disease was confined to the mouth throughout its entire course, and an opportunity to observe the primary lesions was presented in case 1 owing to a recent relapse after the mouth had been normal for three and one-half months

data, we think, force one to believe that at times granular cell myoblastoma may be malignant Ewing[18] expressed the opinion that most myoblastomas are benign

ORIGIN

Originally the theory was evolved that these tumors were degenerative lesions following injury or inflammation or that they arose from embryonal muscle cells Gray and Gruenfeld[19] stated the belief that the evidence for the theory is insufficient except for the tongue tumors The frequent appearance of the growths on the tongue has suggested the possibility of trauma This possibility was also suggested in Khanolkar's case 1, which followed a fall Crane and Tremblay in 1945 stated that "Definite statement as to the histiogenesis of these tumors is probably unwise at this time" Perhaps this opinion represents good judgment for the present

TREATMENT

As to their treatment, practically all authors agree that these tumors are not amenable to radiotherapy If they are recognized, it would seem to be good judgment for one to excise them, widely, if possible Otherwise, it would be well, if possible, for one to excise the growth and cauterize the base, if the lesion is small

The information concerning these tumors certainly suggests to dermatologists and surgeons the more frequent adoption of biopsy, otherwise many of them will not be recognized

CASE 1—N M, aged 71, a retired Naval officer, was admitted with the complaint of a sore on the tongue, of three weeks' duration

The patient had been a heavy pipe smoker for many years and had but recently noticed this spot on the tongue He did not remember having bitten himself

Physical examination revealed on the left side of the tongue, about halfway back and slightly toward the ventral aspect, a small, somewhat indurated, pearly white lesion, about 6 mm in diameter The area was slightly tender

With the use of local anesthesia the entire lesion was widely excised for biopsy and the base thoroughly destroyed with electrocautery The patient has been followed for two years and shows no evidence of recurrence of the lesion

The histologic report stated that the paraffin section stained with hematoxylin and eosin included buccal mucosa, a zone of atypical cells and underlying skeletal muscle The mucosa was hyperplastic, and irregular pegs extended deeply There was keratinization of groups of the deeper cells The cells were mature Mitoses in the epithelium were rare There was slight parakeratosis Pseudoepitheliomatous proliferation was striking

18 Ewing, J Neoplastic Diseases A Treatise on Tumors, ed 4, Philadelphia, W B Saunders Company, 1940

19 Gray, S H, and Gruenfeld, G E Myoblastoma, Am J Cancer **30** 699-708 (Aug) 1937

The primary lesions of *pyostomatitis vegetans* are noted as flat minute miliary abscesses on a slightly raised dark red inflammatory base The abscesses are *uniform in size*, suggesting early miliary tubercles, and tend to be more or less conglomerate, about 2 to 3 mm apart The process spreads within a very few weeks to involve the whole mouth, including the mucosa of the cheeks, the vestibule, the gingivas, the lingual aspects of the lips, the hard and soft palates and, to a limited degree, the margins of the tongue

As the condition develops chronically, the buccal mucosa begins to proliferate, is thrown into folds and assumes a verrucous appearance The miliary abscesses persist as fixed lesions and are found on the summits of the rugae and in the deep invaginations The mucosa is swollen, red and soft to palpation Under the dental plate in case 2 the miliary abscesses tended to rupture, leaving erosions with an accumulation of exudate becoming sticky from admixture with saliva This exudate could be peeled off, especially in the morning after inspissation from mouth breathing Smears from the miliary abscesses in the early stages show up to 30 per cent eosinophils and the remainder polymorphonuclear leukocytes

Only mild subjective symptoms occurred in each case, and the swollen verrucous lesions were not tender to the touch The verrucous mucosa acted as an insulating surface, and the ingestion of hot or spicy foods was not associated with any unusual discomfort In each case the course was relatively benign and of unusual chronicity with only slight periods of remission

The lesions of the oral mucous membrane were very distinctive and not simulated by those of any other oral disease

Although not a direct etiologic factor, the chronic diarrhea in 2 cases played an important role in lowering the resistance of both patients Both patients could be considered as below normal in their general health, and both had had recent acute infections, in case 2 the oral eruption appeared just after the attack of diarrhea had cleared up

The improvement in the oral disease in both cases was related to the use of liver and iron, together with prolonged vacations, rather than to any local treatment to the mouth

The cutaneous lesions in case 2 suggested an inoculation from the primary lesions in the mouth, but this was not proved The rapid spread of the vegetating cutaneous lesion of the groin was very striking and gave the clinical appearance of blastomycosis cutis The histologic picture was essentially the same as in the specimens removed from the mouth When the patient was hospitalized after three months of local treatment, the cutaneous condition responded to local antiseptic

Atypical cells extended from the inferior border of the epithelium, with which they were in immediate contact, to the underlying skeletal muscle They formed a broad sheet within which were occasional slender septums of connective tissue cells and capillaries Deeply, they mingle with the muscle fibers There were groups consisting in part of striated muscle fibers and in part of atypical cells The diameter of the atypical cells was larger than that of the muscle fibers, but these cells had the same general shape and had sharply outlined boundaries The cytoplasm was pale and finely granular and occasionally contained acidophilic clumps, in some instances they formed fine, parallel, linear, closely arranged, fibrillar lines Cross striation was not identified The nuclei were small but



Fig 1 (case 1)—Myoblastoma of the tongue, with pseudoepitheliomatous hyperplasia of mucosa, × 86

tended to be larger and more rounded than those of normal striated muscle They showed faint, weblike chromatin and, occasionally, a pale pink dot resembling a nucleolus Mitoses were not seen The atypical cells appeared to extend beyond the deep margin of excision

A frozen section showed no sudanophilic droplets in the cells

CASE 2—V B, a Negro woman aged 41, was first seen in April 1946, complaining of a small lump on the left side of her tongue The mass had been first noticed one year previously, was asymptomatic and had been slowly enlarging

The history, except for that of syphilis, which had been well treated, was not relevant

treatment together with radiation therapy There has been no recurrence of the cutaneous lesions in case 2 after several months, although a residual palatal process still persists

It was the cutaneous eruption in case 2 which made it possible finally to clarify the diagnosis of the oral disease in all the cases

BACTERIOLOGY

Smears and cultures from the oral cavity were taken in all cases and also from the cutaneous lesion in case 2 The following report was submitted by Dr Ralph Wheeler, Department of Bacteriology, Tufts College Medical and Dental Schools

CASE 1—Fresh unstained preparations showed numerous pus cells, desquamated epithelial cells, a few red cells and no amebas The dark field was negative for spirochetes Smears showed gram-negative diplococci and short bacilli as the predominating organisms A few gram-positive diplococci were seen, but acid-fast organisms were not demonstrated Wright stain showed 11 per cent eosinophils, but no Leishman-Donovan bodies Vincent's organisms were not found. Cultures on blood agar plates and anaerobic cultures showed a variety of organisms consistent with the normal oral flora, the predominating micro-organisms being gram-negative diplococci, gram-positive micrococci, nonhemolytic enterococci, streptococci of the viridans group and a single colony of aerobic actinomycetes, probably a normal inhabitant

CASE 2—Essentially the same general bacterial flora was found as in case 1 A long gram-negative filamentous organism was found but not identified Saliva filtrate inoculated into the allantoic membrane of chick embryo produced no growth Cultures from the miliary abscesses from the lesion of the skin of the groin showed Staph aureus with a few colonies of hemolytic streptococci

CASE 3—The cultures from the lesions in the oral cavity showed the predominant organism to be a streptococcus of the viridans group There were no beta hemolytic streptococci found on culture

It can be concluded that these findings, together with the clinical course of the disease, indicate that the oral and cutaneous manifestations are not related to the micro-organisms demonstrated

PATHOLOGY OF ORAL AND CUTANEOUS LESIONS

SIX biopsies in all were made from the oral lesions in all cases and one from the verrucous lesion of the skin in case 2

The general histologic pictures observed in these specimens were essentially the same The cutaneous lesions showed more pronounced hyperkeratosis with more extreme acanthosis and developed deeper invaginations of the surface epithelial layer. There was a more pronounced cellular infiltration with more numerous eosinophils in the upper part of the cutis and relatively larger miliary abscesses The oral lesions showed a marked acanthosis with broadening and elongation of the rete pegs with the epithelial surface thrown into folds, in places showing fairly deep invaginations Infiltrating eosinophil and poly-

On the left lateral border of the tongue, midway between the tip and the base, was a well defined, very firm, nontender tumor This measured 0 8 by 0 7 by 0 5 cm , was almost white and had a rough, somewhat verrucous surface Other oral mucosae were normal, but the teeth were extensively carious



Fig 2 (case 2) —Myoblastoma of the tongue, superficial part of tumor, with pseudoepitheliomatous hyperplasia, × 86

The entire lesion was widely excised and the base thoroughly cauterized Eighteen months later the patient was entirely cured

Histologic examination revealed this section to be almost identical with that for case 1 The atypical cells had the same distribution and appearance It was noted that some cells showed a mixture of appearances, in part resembling normal sarcoplasm At the periphery or at one side the cytoplasm might be

morphonuclear leukocytes were noted in the deeper epidermal epithelium A very striking and distinctive picture was the presence of epidermal miliary abscesses with the predominating cell the polymorphonuclear coarsely granular eosinophil leukocyte Focal areas showing epithelial thinning with necrosis at the site of rupture of miliary abscesses were present The tunica propria showed a very marked cellular infiltrate, chiefly eosinophilic, especially in the region of the papillae Deeper in the specimens the cellular infiltration was slight to moderate In addition to the cellular infiltration of the tunica propria, there was considerable edema with increased capillary vascularity Proliferation of the endothelium in the young blood vessels was noted

The over-all picture was that of a granulomatous inflammatory process with unruptured miliary epidermal abscesses and focal areas of surface necrosis The tissue and blood eosinophilia was striking in 2 cases, although not diagnostic, as eosinophilic infiltration of tissue lesions and the presence of eosinophils in the peripheral blood stream are commonly observed in pemphigus vegetans, dermatitis herpetiformis and other dermatoses

DIFFERENTIAL DIAGNOSIS

When first seen and for several months afterward the disease involving the oral cavity remained undiagnosed, and it was only after the characteristic verrucous lesion of the skin in case 2 developed that a definite diagnosis was made

In pemphigus vegetans, oral lesions are characterized by a primary flaccid bullous lesion which contains a serous fluid tinged with blood These bullae rupture early, leaving superficial painful eroded areas New lesions continue to form, and the oral condition presents a characteristic appearance Desquamated epithelium and a fibrinous exudate frequently coat the superficial ulcerations In very chronic oral involvement, focal areas of proliferating granulation tissue may develop but the process is very painful

In the very rare oral disease oral pemphigus, in which the lesions are confined to the mouth, the primary lesions are also bullous and the process may continue for years Extension to the pharynx may occur in these cases, and pain is a prominent symptom

Dermatitis herpetiformis has been described as a disease that may cause cutaneous lesions similar to those described in pemphigus vegetans Oral involvement in dermatitis herpetiformis has been described, with lesions essentially the same as in pemphigus vegetans However, many dermatologists state definitely that the mouth is not involved in this disease, and I have never seen a single case of dermatitis herpetiformis with oral lesions

brightly eosinophilic and compact, as in normal striated muscle cells, while centrally or at an opposite side it was loose, pale and granular Cells of intermediate intensity of staining were also present They had loose fibrils and faint cross striations and resembled skeletal muscle except that they were larger and paler No mitoses were present The atypical cells extended to the depth of the section The epidermis was similar in every respect to the section from case 1



Fig 3 (case 2) —Myoblastoma, deep portion of tumor, in which may be seen mixture of the granular cells with the striated muscle of the tongue, × 134

There was more parakeratosis, however, and an extreme pseudoepitheliomatous hyperplasia

CASE 3[20]—L S, a man aged 40, had had a gradually developing tumor in the anteropalmar aspect of the distal phalanx of the right thumb for four years

20 Included through the courtesy of Dr J M Hamilton and of Dr D J Rehbock, clinical pathologist, St Vincent Charity Hospital

Lupus erythematosus not infrequently shows buccal lesions which tend to ulcerate early and usually are associated with subjective symptoms of pain and soreness, although some patients are relatively free from pain The lesions are sharply defined and their appearance varies with the age of the lesion The common locations are on the lips and in the vestibule of the mouth, especially in the molar regions The palate and gingivas, together with other locations, may be involved The lesions in the beginning are bright red plaques with slightly infiltrated borders, with thinning of the centers as the lesions progress Many of these lesions as they heal resemble those of leukoplakia

Eosinophilic granuloma,[18] regarded by many as an entity, has in recent years been described in the dermatologic literature The complexity of the clinical picture and a more specific histologic picture help to differentiate this condition from the oral and cutaneous lesions of pyostomatitis vegetans To date there has been no mention of oral lesions in all the cases of eosinophilic granuloma reported in the literature

TREATMENT

As indicated in the description of these cases, local therapy had no effect in clearing up the lesions Local and parenteral administration of penicillin and oral administration of sulfonamide drugs had no beneficial effect on the mucosal lesions Use of iron and liver together with prolonged vacations was effective in aiding the return to normal of the buccal mucosa in case 1, and in case 2 a similar result was accomplished except for a residual process on the palate after twenty-two months In case 3, according to the most recent report, in 1947, there was improvement in the oral condition with a residual process still persisting in the palate region

SUMMARY

Three cases of a rare vegetating oral mucosal disease are described in 1 of which typical pyodermatitis vegetans developed, in the others the condition remained as an oral entity

Pyostomatitis vegetans presents a characteristic and distinctive oral disease with primary miliary abscesses on an inflammatory base with the development of verrucous changes

The clinical course in 2 cases was confined to the oral cavity, these are the only cases reported in the literature in which the disease remained an oral entity

18 Weidman, F M The "Eosinophilic Granulomas" of the Skin, Arch Dermat & Syph **55** 155 (Feb) 1947 Lewis, G W, and Cormia, F E Eosinophilic Granuloma, ibid **55** 170 (Feb) 1947 Lever W F Eosinophilic Granuloma of the Skin, ibid **55** 194 (Feb) 1947

The tumor was freely movable and completely painless There was a history of catching the thumb in a door jamb and pinching it severely some months before In fact, the injury had been so severe that the patient had only a spoon nail on that digit. His occupation was not relevant

The tumor was only recently excised through an incision of the skin without removal of skin There were no other lesions

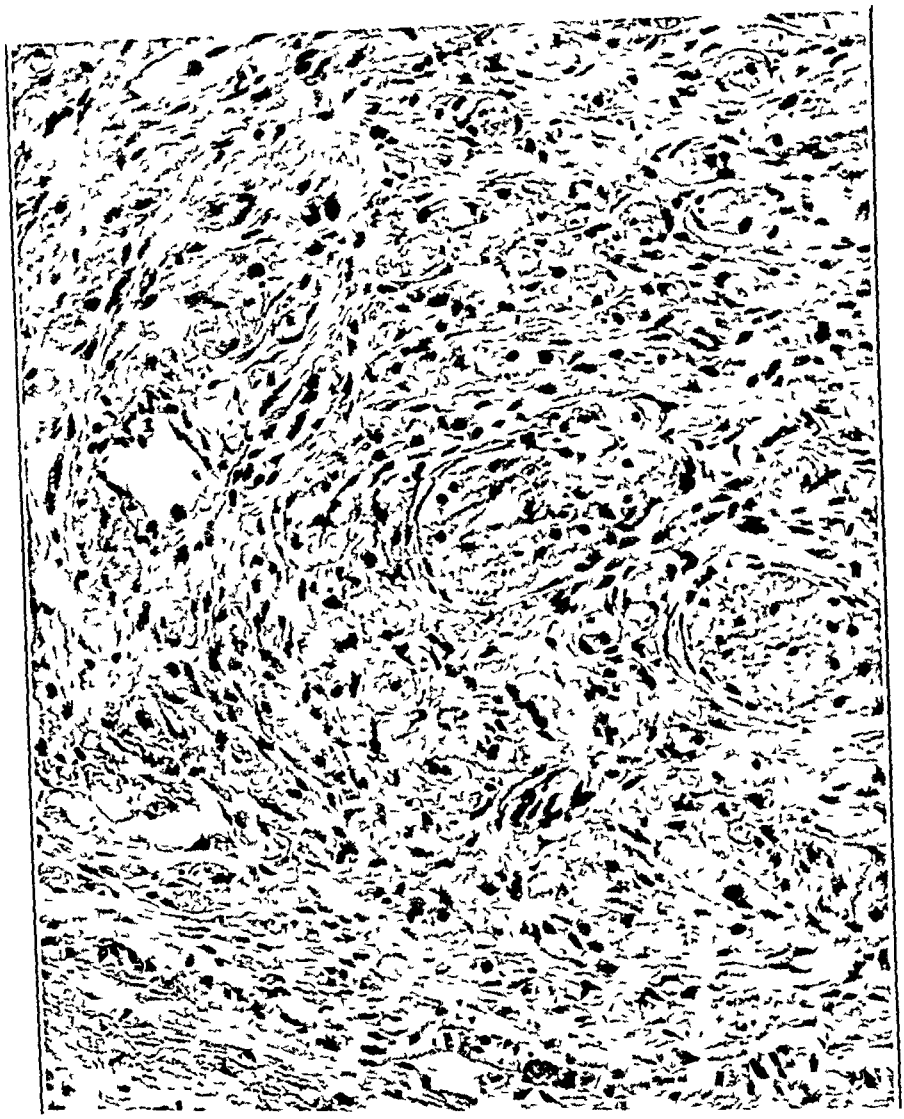


Fig 4 (case 3) —Granular cell tumor of finger, with coarse granularity of cells, about × 200

The specimen consisted of an ovoid, firm, pearly gray tissue mass, measuring 1 0 by 0 6 cm The surface was lobulated but otherwise smooth Section revealed a firm, fibrous, pearly gray tissue

The paraffin section stained with hematoxylin and eosin consisted largely of rounded groups of atypical cells enclosed by a circle of fusiform cells and hyaline fibers These groups were in turn collected and held together by interlacing bands of hyaline fibers, and the entire mass was bounded by collagenous tissue on two sides Outside of this capsule were a little areolar tissue and a few sweat glands The other two sides were cut surfaces

In case 2 a complicating vegetating dermatitis developed, the pathologic picture presenting the same changes as were found in the oral lesions in the 3 cases

The oral lesions were resistant to local oral therapy in all cases, but the cutaneous lesion responded to antiseptic and radiation therapy

Bacteriologic study of the oral lesions in all 3 cases revealed no specific micro-organisms or virus

A similarity to pemphigus vegetans is indicated, but the clinical course with characteristic oral lesions indicates a definite disease entity involving the oral cavity

The atypical cells were round and polyhedral or long and cylindric They were granular and moderately eosinophilic The granules were fine, although a few coarse hyaline clumps were seen Indistinct cross markings were seen Some of these appeared as very fine basophilic lines, and others had an appearance produced by parallel arrangement of granules Some nuclei were basophilic, compact and small Others were larger and showed a reticular and punctate chromatin pattern Single or multiple nuclei might be seen in a single cell Where cells were longitudinally cut, spaced nuclei might be seen in a row Mitoses were not present

COMMENT

In the two lingual lesions there were transitions from striated muscular cells to granular atypical cells (fig 3) It is reasonable to conclude that for these the term myoblastoma is justified

In case 3, however, there were differences The cells were larger and more coarsely granular, and there was grouping in round nests, in contrast to the uniform sheets found in the lingual lesions Muscular relations were not seen Further, the tumor arose in a site away from normally situated skeletal muscle The histologic diagnoses entertained were myoblastoma, traumatic pseudoneuroma and neurofibroma The first-mentioned one seemed the most likely

At this juncture the presentation of Fust and Custer [21] concerning granular cell neurofibroma was heard, and the slide was sent to them for an opinion They expressed the opinion that it was an example of granular cell neurofibroma

Without further study concerning the nature of these tumors, and pending the publication of Fust and Custer's work, we choose to call the lesion a granular cell tumor and to be noncommittal concerning its origin

SUMMARY

A report is made of 2 cases of granular cell myoblastoma of the tongue and of a subcutaneous granular cell tumor of the thumb They are discussed from a clinical and microscopic standpoint

Such tumors are probably much commoner than is suspected

The tumors are found most frequently on the tongue and in the mouth and appendages, they are seen next most frequently on the skin and subcutis

While in most cases these tumors are not malignant, nevertheless sufficient reports are accumulating to indicate that in certain locations and under certain conditions invasion, metastases and death may result from less than total surgical removal The tumors are highly radioresistant

21 Fust, J A, and Custer, R P The Neurogenesis of So-Called Granular Cell Myoblastoma, Am J Clin Path **19** 522-535 (June) 1949

NONLIPID GRANULAR CELL TUMORS

HAROLD N COLE, M D
AND
HERBERT LUND, M D
In Collaboration with H N Cole Jr, M D, J R Driver, M D, Richard C Light, M D, and Don R Printz, M D
CLEVELAND

NONLIPID granular cell tumors are usually considered to be myoblastomas, and in the following review this term will be used freely However, identity of all these tumors is still open to question We present 3 cases exemplifying this problem

In 1926 Abrikossoff [1] reported a tumor of myoblasts occurring chiefly in relation to striated muscle He thought it might be due to degenerative lesions following injury or inflammation In 1931 [2] he further elaborated his ideas on myoblastic myomas, as he called them, feeling that perhaps they were made up of embryonal elements primitive myoblasts He divided them into four different types, of which the first three are all granular cell and benign (1) round, egg-shaped or elongated myoblasts, 20 to 25 microns in length, showing granules but no longitudinal or cross striations, (2) growths in which some of the cells may show longitudinal or cross striations, and (3) a hypertrophic form with cells 40 to 160 microns in length and at times multinucleated. He also described a further type (4), in which the myoblasts are not granular but atypical, which resembles more a polymorphous sarcoma

Crane and Tremblay,[3] in reporting 5 cases in 1945, pointed out that, although Abrikossoff had reported 5 cases in 1926, Weber in 1854, Hertaux in 1881, Pendel in 1897 and Moschcowitz in 1922 had described what were apparently identical lesions Crane and Tremblay reviewed

Read at the Sixty-Eighth Annual Meeting of the American Dermatological Association, Inc, San Diego, Calif, April 28, 1948

From the Department of Dermatology and Syphilology and from the Institute of Pathology of the Western Reserve University School of Medicine and of the University Hospitals

1 Abrikossoff, A Ueber Myome ausgehend von der quergestreiften willkurlichen Muskulatur, Virchows Arch f path Anat **260**·215-233, 1926

2 Abrikossoff, A I Weitere Untersuchungen uber Myoblastenmyome, Virchows Arch f path Anat **280** 723-740, 1931

3 Crane, A R, and Tremblay, R G Myoblastoma (Granular Cell Myoblastoma or Myoblastic Myoma), Am J Path **21**·357-375 (March) 1945

There are a few cases in which these growths have been multiple in type on the skin and subcutis as well as in internal organs

In tumors of the skin and mucous membrane, the pseudoepitheliomatous hyperplasia is frequent enough to be noteworthy

The tumors of the tongue strongly suggest muscular origin Other tumors without demonstrable transition from or location in muscular tissue are more obscure The work of Fust and Custer is anticipated

1352 Hanna Building (15)
2085 Adelbert Road (6)

ABSTRACT OF DISCUSSION

DR HAMILTON MONTGOMERY, Rochester, Minn I have been interested in myoblastoma ever since Dr Machacek called my attention to this condition several years ago when the American Academy of Dermatology met in New York A fellow in pathology at the Mayo Clinic, Dr G H Murphy, just finished studying 10 cases which he classified under the headings of the uniform type of myoblastoma, which is benign, and the pleomorphic type, which is essentially a rhabdomyosarcoma The granular cells appear in both types I had formerly accepted the concept that granular cell myoblastoma arose from skeletal muscles Recently, however, I have seen 2 cases in which there apparently was origin from smooth muscles In 1 case there was a lesion on the vulva of a Negro woman aged 72, which showed smooth muscle origin Material from a recent case with involvement of the anal region, sent to me by Dr Wasserman of Cincinnati, showed granular myoblastoma cells apparently arising in relation to the walls of the capillaries in the papillary bodies This observation would suggest endothelial origin, because these capillaries are not supposed to have a muscular coat In some of Murphy's cases of the pleomorphic type, there was a history of trauma preceding the development of the tumor and subsequent metastasis and death Myoblastoma does not have a typical clinical appearance but does have a characteristic histologic one

DR ANTHONY CIPOLLARO, New York My attention was brought to this disease several years ago when a patient came to my office with a small lesion on the tongue I diagnosed it as a fibroma I was going to infiltrate it with procaine hydrochloride (novocain®) and destroy it with electrodesiccation, but, because the man was worried about cancer, I removed the tissue and submitted it for biopsy The type of lesion was not recognized by the first dermatopathologist It had unusual cells with which I was not familiar Dr Richter, a general pathologist, immediately diagnosed it as a granular cell myoblastoma This case was published by me a few months ago in the ARCHIVES [12]

I think that all nodular lesions of the tongue should be removed and submitted to the laboratory for histologic study

DR. LOUIS WINER, Hollywood, Calif Recently my associates and I had submitted to our laboratory a piece of tissue which showed myoblastoma The differential stains were very interesting Van Gieson stain colored the blastoma tissues yellow, like smooth muscles Mallory's stain showed the tissue to be bright red, just as it does muscle fibers Therefore, I would advise that differential staining be done In the case of neurofibromatosis, also, differential stains would be of benefit because the tissue in neurofibromatous structure is mostly fibrous and stains like connective tissue, red with Van Gieson and greenish blue with Mallory's stain

the literature, which up to the time of their publication consisted of 162 cases, 34 of the skin and subcutis and 61 of the tongue

In the past few years there has been much more interest directed to this group of tumors, with quite extensive reports, among others those by Klemperer,[4] Howe and Warren,[5] Ravich, Stout and Ravich,[6] Powell [7] and Khanolkar [8] Reports on the disease, as it has become better known, have mounted rapidly, thus Powell reported 4 cases in 1946, Simon,[9] 6 in 1947, Khanolkar, a further 10 in September 1947, and Allen,[10] 27 in 1948 The total, including Bloom and Ginzler's,[11] Cipollaro and Einhorn's [12] recent cases and our 3 cases, is around 214 cases It is our view that as the entity becomes better known and as the physician becomes more inclined to examine lesions histologically, granular cell myoblastoma will be found to be far from a rare entity Thus Allen found 27 myoblastomas in material from 8,000 specimens of cutaneous diseases collected in World War II by the Army Institute of Pathology

LOCALIZATION AND CHARACTERISTICS

These tumors seem to be found most frequently on the tongue and in the mouth and larynx, in about some 37 per cent of the cases The growths have been distributed all over the body and in some internal organs

Strangely enough, the occurrence of these tumors in the second most frequently involved area, the skin and subcutis, has not been sufficiently emphasized until in the very recent literature Powell in 1946 stated that 20 4 per cent of the cases so far reported had involved these structures In 3 of her 4 cases the cutaneous surfaces were affected—

4 Klemperer, P Myoblastomata of Striated Muscle, Am J Cancer **20** 324-337 (Feb) 1934

5 Howe, C W, and Warren, S Myoblastoma, Surgery **16** 319-347 (Sept) 1944

6 Ravich, A, Stout, A P, and Ravich, R A Malignant Granular Cell Myoblastoma Involving Urinary Bladder, Ann Surg **121** 361-372 (March) 1945

7 Powell, E B Granular Cell Myoblastoma, Arch Path **42** 517-524 (Nov) 1946

8 Khanolkar, V R Granular Cell Myoblastoma, Am J Path **23** 721-739 (Sept) 1947

9 Simon, M A Granular Cell Myoblastoma, Am J Clin Path **17** 302-313 (April) 1947

10 Allen, A C Survey of Pathologic Studies of Cutaneous Diseases During World War II, Arch Dermat & Syph **57** 19-56 (Jan) 1948

11 Bloom, D, and Ginzler, A M Myoblastoma, Arch Dermat & Syph **56** 648-658 (Nov) 1947

12 Cipollaro, A C, and Einhorn, M B Granular Cell Myoblastoma, Arch Dermat & Syph **56** 812-818 (Dec) 1947

DR HARRY ARNOLD JR, Honolulu, Hawaii I should like to mention in this connection an instance of a small lesion on the side of a young woman's neck, clinically an obvious granuloma pyogenicum, which was sectioned in our laboratory purely as a routine matter and turned out to be an infiltrating, anaplastic, granular cell carcinoma, the cells of which were full of fat It was an example of the sort of lesion Dr Cipollaro spoke of, which is all too frequently merely thrown away after its removal Excision of the operative site the following afternoon revealed a nest of residual neoplasm

DR HAROLD N COLE, Cleveland Thank you all for the discussion I mentioned a classification of these tumors containing four groups The fourth group is that of a nongranular polymorphic sarcoma, generally not accepted as a granular cell myoblastoma, and should be deleted

in 1 with multiple lesions Tuta and Schmidt[13] in 1942 reported 3 examples of cutaneous involvement and 1 of the trapezius muscle Ebert and Slepyan[14] the next year presented a patient before the Chicago Dermatological Society with a small nodule on the dorsum of the left hand In the discussion Becker[15] stated that he had recently seen in consultation with Dr Clarence Shaw a similar tumor on the upper part of the chest Then Bloom and Ginzler reported the case of a Negro woman with a hazelnut-sized, round, raised tumor of the lip which, after endothermy, was followed two years later by a hazelnut-sized nodule of the skin and subcutis of the right thigh, a similar lesion on the trunk and a smaller one on the right hip Very recently Cipollaro and Einhorn observed a marble-sized nodule of the right index finger as well as one on the tongue There have been a few instances reported of polyp-like masses in the ear canals, which growths may attract attention by bleeding

These tumors are very often symptomless, are many times sessile and vary in size from 0 5 to 2 0 or 3 0 cm , occasionally being even larger Their color on the mucous membrane is often described as grayish or opalescent In Ebert and Slepyan's case the quarter-sized mass was made up of several smaller nodules Rarely are the growths painful unless in a vital structure and ulcerating as well The patients vary from newborn babes with small lesions of the alveolar processes up to persons in the second, third or fourth decade of life, rarely older

MICROSCOPIC APPEARANCE

These tumors are generally well circumscribed, ovoid or lobulated and rather firm Occasionally the borders may show outlying islands of cells and may even penetrate surrounding tissues The growths are made up of rather large, elongated or polyhedral cells, appearing as single cells or in sheets They may have a banjo or tadpole shape or the shape of a tear drop, as has been mentioned by many writers And some tumors will show a striking pseudoacinar appearance of the cells They have a coarse, granular cytoplasm, acidophilic in character, and nuclei that are comparatively small and have an angular appearance In some cases the cells may be multinucleated The cytoplasm is often foamy, resembling somewhat that of a xanthoma cell However, it does not have the tinctorial reactions of the latter Occasionally the cells

13 Tuta, J A , and Schmidt, F R So-Called Myoblastoma, Arch Dermat & Syph **46** 225-233 (Aug) 1942

14 Ebert, M H , and Slepyan, A H So-Called Myoblastoma, Arch Dermat & Syph **48** 348-349 (Sept) 1943

15 Becker, S W , in discussion on Ebert and Slepyan[14]

USE OF REPELLENTS IN CLINICAL DERMATOLOGY

General Principles

LEON GOLDMAN, M D
CINCINNATI

AMONG the advances in preventive medicine in the last world war were the detailed studies in the chemical control of insects As yet, the practicing physician, as compared with the military physician does not appear to be fully aware of the possibilities for the control of insects, especially the disease-bearing types This chemical control, in general, falls into two phases insecticidal and repellent activity

The development of insecticides is well known from the advances in the preparations of pyrethrins and DDT (2,2-bis [p-chlorophenyl]-1,1,1-trichloroethane) and its newer analogues, such as DDD (1,1-dichloro-2,2-bis-[p-chlorophenyl]-ethane) and methoxychlor (1,1,1-trichloro-2,2-bis [p-methoxyphenyl]-ethane Perhaps less is known about the developments of new insecticidal materials, which include such substances as gammexane® (hexachlorocyclohexane), velsicol 1068® (also called chlordan), hexaethyltetraphosphate, piperine compounds, parathion (0,0-diethyl-0-p-nitrophenyl thiophosphate), very toxic, phenyl cellosolve® (ethylene glycol monophenyl ether) and eura® (10 per cent crotonyl-N-ethyl-ortho-toluidide) [1] Dermatologists should be interested also in the development of effective modern rodenticides, such as 1080, alpha-naphthyl-thiourea, and fanyline

Repellents have a distinct and important value because they serve, by means of a protective cloud of volatile products about the person, by taste mechanisms, by physical or mechanical means, etc, to keep insects away Repellents are necessary, for it may be possible for one to be bitten during the latent period of activity of an insecticide At present, it is not possible to combine in a single universally effective mixture both insecticidal and repellent properties Prior to World War I, few, if any, effective repellent materials were available Smokes and oil of citronella were old favorites During World War II thousands of compounds [2] were tested, and continued to be tested, for their repellent and toxic qualities against mosquitoes, lice, mites, ticks and "other

From the Department of Dermatology and Syphilology of the University of Cincinnati College of Medicine

1 Heyroth, F Personal communications to the author

2 Travis, M, and Cochran Insect Repellents Used as Skin Treatment by the Armed Forces, J Econ Entomol **39** 637, 1946, Chem Abst, vol 41, no 2207

in certain tumors will show suggestions of longitudinal or cross striations Keynes [16] and Klemperer pointed out the interesting feature of overgrowth of the overlying epithelium where the skin or mucous membrane is concerned—a pseudoepitheliomatous hyperplasia This condition was striking in the cases of Bloom and Ginzler, even to the production of pearls, which the pathologists interpreted as indicative of a low grade squamous cell carcinoma

MALIGNANT GRANULAR CELL TUMORS

Originally, Abrikossoff separated a fourth group of tumors resembling more a polymorphous sarcoma, which is quite generally not included in the classification of granular cell myoblastomas Howe and Warren reported that they had seen 10 cases, among which there were 5 with definite malignant properties, 3 of the growths metastasizing to the lung They also stated that they had found 10 cases in the literature and 4 of their own with either gross or microscopic evidence of local invasion There had been regional adenopathy in 7 cases, but in only 3 were metastases to lymph nodes proved by biopsy In none was there response to irradiation Ravich, Stout and Ravich expressed the opinion that all 5 of their cases should be put in Abrikossoff's fourth class They were skeptical of the malignant character of this tumor until the occurrence of their own case, in which a tumor of the bladder recurred after excision and in which the patient died eleven months later from metastases They stated the belief that their case is the first example of a type 3 tumor metastasizing and causing death However, in Morpurgo's [17] case the patient, with a tumor of the tongue, died with metastases in the cervical nodes In Powell's patient 3, who had a large growth in the floor of the mouth, displacing the tongue, there was invasion of the tissues and death from erosion of a vessel Moreover, in her case 4 there were tumors in the scalp, the upper eyelid, the lower lip, the right axilla, the right side of the torso, the left thigh, the vulva, the back, the toe and the buttock, as well as of the uterus and an ovary After removal of some of these, including the uterine and ovarian growths, further growths developed on the skin This development of further cutaneous lesions also occurred in Bloom and Ginzler's case after partial removal of the tumor of the lip Moreover, Khanolkar, in a recent article, reported a further 10 cases in which there could be no uncertainty regarding the neoplastic nature These

16 Keynes, G Rhabdomyoma of Tongue, Brit J Surg **13** 570-572 (Jan) 1926

17 Morpurgo, B Myoblastomi, Arch per le sc med **59** 229-252 (Feb) 1935, cited by Bloom and Ginzler [11]

arthropods affecting the health of man" [8] The brilliant researches of the various governmental groups are especially known by the studies on DDT However, equally important work has been done, and continues to be done, especially by the Bureau of Entomology and Plant Quarantine of the Agricultural Research Administration, in the investigation of repellents Effective mixtures, well known to military physicians, were the dimethylphthalate solutions and the dimethylphthalate combined with hexanediol and indalone® (butyl ester of 3,4-dihydro-2,2-dimethyl-4-oxo-1,2-pyran-6-carboxylic acid) Toward the end of the war, Pijoan [1] and Jachowski,[1] working at the Naval Medical Research Institute, developed the NMRI-448 repellent This compound represents the four hundred and forty-eighth attempt to find an effective repellent mixture, which essentially was the combination of 70 per cent 2-phenylcyclohexanol and 30 per cent 2-cyclohexylcyclohexanol Jachowski [1] claimed that NMRI-448 is superior to the 612 and the 622 mixture in effectiveness against the mosquitoes of tropical America and of equal effectiveness against the mosquitoes of the United States and Alaska Recent work has indicated that N-propyl-N,N-diethylsuccinamate has also good repellent action when applied to the skin Recent work by Brennan [3] has also included the development, especially as a repellent for ticks (Dermacentor andersoni, Amblyomma americanum), of phenylcyclohexanol and butylacetanilide Our preliminary studies with N,n-butylacetanilide indicate that this material is also of low sensitivity index

With regard to the protection of the person, the two significant features of repellent activity are, first, the limitation of the protection to the area or areas to which the repellent has been applied and, second, the duration of activity of the repellent action In general, the repellent mixture in a suitable vehicle may be used locally on the skin, or clothing may be impregnated with it The duration of the activity varies with the type of repellent, and perhaps with the type of vehicle The recent development in the use of repellents has increased the time of repellent activity to approximately eight hours for the NMRI-448 group Clothing impregnation prolongs the period of repellent activity Against ticks, the repellent activity is said to last as long as twelve days

Repellents in dermatologic practice are useful specifically in preventing chigger infestation and bites, mosquito bites, fly bites and flea bites, they act as a tick repellent and possibly are of value in management of the familial infestations pediculosis and scabies

Protective clothing and various types of sulfur preparations have been used to prevent chigger (genus Trombicula) infestations In

3 Brennan, J M Preliminary Report on Some Organic Materials as Tick Repellents and Toxic Agents, Pub Health Rep **62** 1162, 1947

consisted of local granular necrosis with cellular debris surrounded by many epithelioid cells and a few connective tissue cells, I was inclined to consider the case as one of granuloma annulare, although the patient did not have any ring lesions I have seen a few patients with granuloma annulare with scattered papules, but they also had the typical annular lesions However, Hartzell (*J A M A* **63** 230 [July 18] 1914) and Stillians (*J Cutan Dis* **37** 580, 1919) each reported a case of granuloma annulare without ring lesions, and the latter mentioned many others who had observed similar cases

The patient has definite lichenoid papules, some resembling lichen planus, although the lesions are softer to the touch than those in lichen planus There is no moniliform arrangement and no waxy papules as were described in lichen moniliformis Another interesting point in this case is that the patient has diabetes but clinically the lesions do not suggest necrobiosis lipoidica diabeticorum, and histologically one often finds extensive vascular damage in necrobiosis as well as in lichen moniliformis, features not found in this case and usually not seen in granuloma annulare In consideration of all this, I am inclined to consider this as a case of granuloma annulare

Xanthoma Tuberosum Presented by Dr L M Fruchtbaum

Epithelioma of the Cheek in a Woman Aged Twenty Years Presented by Dr Seymour H Silvers

Acrokeratosis Verruciformis of Hopf Presented by Dr C B Locasto

M C, a Negro woman aged 52, stated that she has had thick skin on the palms and soles and wartlike growths on the back of her hands since birth There are no subjective symptoms The palmar and plantar surfaces are hyperkeratotic The dorsal aspects of the hands and feet and the distal parts of the forearms are studded with numerous, discrete, confluent and flat-topped verrucalike polygonal papules The nails are frayed distally, have vertical linear striations and are brittle

DISCUSSION

Dr Joel Schweig This is an unusual case and of a type rarely seen at our meetings I agree with the diagnosis Acrokeratosis verruciformis and epidermodysplasia verruciformis are different in that the latter appears in persons with consanguineous parents and is associated with malignant degeneration of the lesions The concept of this condition is that it is of nevoid character

Tinea Capitis in an Adult (Microsporon Lanosum) Presented by Dr E A Gauvain

T A, a widow aged 73, had been losing hair for four months She complained of slight itching of the scalp She had no recollection of direct contact with dogs or cats, but a dog had been a recent visitor to one of her neighbors

The hair of the scalp is thick and long, with many areas showing slight erythema and definite defluvium without any sharply defined areas of alopecia Under the Wood light, fluorescent hairs mingled with nonfluorescent hairs are seen throughout the scalp A culture of infected hair grew Microsporon lanosum

CHICAGO DERMATOLOGICAL SOCIETY

Francis W Lynch, M D, *President*

Leonard F Weber, M D, *Secretary*

Feb 19, 1947

Pemphigus Vulgaris Presented by Dr M H Ebert and (by invitation) Dr N L Baker

A Case for Diagnosis (Erythema Perstans?). Presented by Dr T Cornbleet and (by invitation) Dr D Cohen and Dr J Graffin

Lupus Pernio? Presented by Dr S Rothman and (by invitation) Dr Z Felsher and Dr L Rubin

Sarcoidosis, Keloidal Nodules on the Nose of a Young Negro Woman Presented by Dr H Rattner and (by invitation) Dr H Rodin and Dr J Graffin

A Case for Diagnosis (Lupus Erythematosus in a Girl of 17 Years). Presented by Dr D Omens, Dr S J Zakon and (by invitation) Dr H Omens and Dr J Graffin

Systemic Blastomycosis Presented by Dr D Omens and (by invitation) Dr H Omens and Dr J Graffin

S W, a Negro woman aged 39, on Dec 24, 1946 precipitously delivered a full term baby while on the street Several days later she noticed a few nodules on the right forearm, which gradually grew to form abscesses In the next two months numerous fluctuant, hen's-egg-sized abscesses appeared on the face and extremities, and, in addition, warty lesions developed on the face and trunk For the past few weeks she has had fever, "night sweats," headache and malaise, but no symptoms referable to her gastrointestinal, respiratory or genitourinary tract Until the time she entered the Cook County Hospital, she had nursed her apparently healthy baby Her other four children and her husband have been in good health She has not been out of Chicago in the past two years and has no contact with flowers, gardening or animals

Examination reveals numerous fluctuant, tender, subcutaneous abscesses scattered on the face, extremities and back, varying from 1 to 5 cm in diameter In addition, there are verrucous nodules on the face and trunk Physical examination revealed no other abnormalities While in the hospital she has had a low grade fever daily, accompanied with headache and malaise

The Kahn reaction of the blood was negative The urine was normal The blood examination showed erythrocytes 4,600,000, hemoglobin 67 per cent and leukocytes 22,200 Sterile aspiration of a subcutaneous abscess resulted in recovery of blastomycetes on culture Direct sodium hydroxide preparation revealed numerous round doubly refractile bodies, some of which were budding The blastomycin intracutaneous test revealed a 12 mm erythematous papule at 24 hours, but at 48 hours the papule was only 5 mm in diameter The roentgenogram of the chest revealed a normal cardiothoracic ratio There was a small discrete

recent years, I have used benzyl benzoate preparations on the lower extremities as a protective measure King has indicated that for uniform impregnation against chiggers these five new compounds are all superior to benzyl benzoate, benzyl, 2-thenyl benzoate, p-cresyl benzoate, diphenyl carbonate and 2-thenyl salicylate The modern repellent for the prevention of chigger bites are rubbed in from the ankle to the knee, they are also put into the cuffs of trousers, clothing may be impregnated and the substance rubbed into shoes The technic of this application refers to protection of the person only while he is walking through chigger-infested areas, for sitting or lying in the grass, however, greater areas of the body must be protected Besides the usual severe discomfort from these bites, significant reactions may occur in the elderly, in persons with latent and actual stasis syndromes and in infants and young children with extensive bites Parkhurst [1] emphasized repeatedly the necessity of preventing bites from the chigger For the use of repellents against flying insects, such as flies and fleas, the repellent must be used on the exposed areas of the skin Such areas include chiefly the head, neck, neck line, wrists, arms and trouser line It should be remembered that the repellent must be reapplied if the supposed period of activity has been exceeded When repellents are mixed in "sun tan mixtures," one must consider the possible insect-attracting qualities of these mixtures

For those insects which serve as vectors for disease, such as ticks, mosquitoes, simulia and flies of the Phlebotomus group, these repellents have an importance far beyond the prevention of the mere initial cutaneous bite In a previous report,[4] the relation of the lichen urticatus syndrome in children to bites from insects was shown For those children, repellents are needed, especially against fleas, chiggers and bedbugs Tick repellents also may be applied to the skin or the clothing impregnated Although repellents should have value in familial infestations with Phthirus pubis, Pediculus capitis and Sarcoptes scabiei, few controlled studies on civilian groups are available In practice, actual antiparasiticidal treatment of the entire family, especially in the case of scabies (scabies domestica), is carried out, and the repellents, though less irritating, are not needed

The mixtures of repellents that were developed by the armed services during the war have undergone, in addition to severe critical laboratory use and field trials, controlled tests with regard to systemic

4 Goldman, L Lichen Urticatus Syndrome as a Manifestation of Sensitivity to Bites from Various Species of Arthropods, Arch Dermat & Syph **58** 74 (July) 1948 Draize, J H , Nelson, A A , and Calvery, H O The Percutaneous Absorption of DDT (2,2-Bis [p-Chlorophenyl] 1,1,1-Trichlorethane) in Laboratory Animals, J Pharmacol & Exper Therap **82** 159, 1944

One of our patients was born and remained in San Diego county until his entry in the Navy, while the other was born in North Carolina, his only possible contact with the organism coming while he was stationed in San Diego Lee's [10] experience with certain bodies of troops indicates a high percentage of infections when men are exposed to very dusty conditions in an endemic area The recent drought in California poses an additional hazard in the spread of the infection It has also been shown that animals in endemic areas harbor the infection, and the possibility of a rodent reservoir has been advanced Since the infection is carried in dust, the possibility of dissemination in vehicles and luggage of those traveling in and out of the endemic areas cannot be entirely discounted Although the danger on the present evidence is very slight, it is not yet definitely known whether or not the many thousands who were infected during their training period in an endemic area may have serious complications later in life

SUMMARY AND COMMENT

Much has been added to the knowledge and understanding of coccidioidomycosis in the past decade The endemic areas have been redefined and are known to extend over the southwestern United States and northern Mexico The patients in our cases undoubtedly contracted their infections in San Diego county, which had not been considered an endemic area They were both from dark-skinned races, in whom the progressive disseminated, frequently fatal form is most likely to develop Lesions of the gastrointestinal tract, which are said not to occur but have been recorded in the literature on one other occasion, were found widely distributed in 1 of our cases Although the infection in most instances is entirely benign and complete clinical recovery can be anticipated in even those who have pulmonary involvement with cavitation, possible serious complications may develop in later life in some of the many persons who were infected during their training period in an endemic area during the last war The similarity to and distinction from tuberculosis of this disease will become increasingly important to physicians everywhere, since these men have now returned to their homes throughout the United States Specific treatment is still lacking, and neither drugs nor vaccines have appreciably altered the course of the progressive disseminated form

3367 Fourth Avenue (3)

10 Lee, R V Coccidioidomycosis in the Western Flying Training Command, California & West Med **61** 133 (Sept) 1944

REACTIONS IN TATTOOS (CHRONIC DISCOID LUPUS ERYTHEMATOSUS)

JOHN F MADDEN, M D
ST PAUL

Reactions in tattoos generally fall into one of four groups The reactions in one group consist in the immediate response of the skin to the physical injury of tattooing This is rarely accompanied with or followed by secondary infection In

From the Department of Dermatology, Ancker Hospital, St Paul, Dr John F Madden, Director, and the Division of Dermatology and Syphilology, University of Minnesota Medical School, Dr H E Michelson, Director, Minneapolis

toxicity and cutaneous irritation and sensitivity As an example, to develop a technic of screen testing for rapid elimination of those compounds which would be harmful to man and animals, Draize, Nelson and Calvery [4] devised a detailed percutaneous toxicity test on animals The materials that are available now, as a result of such extensive cooperative work, are mixtures with a low sensitivity index

From experience, it appears that the discomfort suffered with the use of repellents is usually caused by its vehicles, alcohol or other solvents, rather than by the repellents themselves It is the solvent that is responsible for the burning around the eyes and mouth and on active sunburned areas For some time cream vehicles, with a content of liquid repellent varying from 10 to 60 per cent, have been suggested by the Orlando Florida Laboratory of the Bureau of Entomology and Plant Quarantine of the Agricultural Research Administration In general, a cream type of vehicle is preferable

Persons traveling to tropical or subtropical areas should receive, in addition to their protective inoculations, simple and practical instructions regarding the modern uses of insecticides and repellents The dermatologic aspects of modern insecticides will be reported in another article

CONCLUSION

Greater use should be made by the civilian dermatologist of the recent advances in the chemical control of insects Repellents are of value for the prevention of bites, especially in the case of persons who are sensitive to bites of the mosquito, fly, flea, chigger (Trombicula) and the tick Persons traveling in foreign countries and in tropical or subtropical areas should be instructed in the chemical control of insects This instruction is as important as the detailed inoculation program The activity of the repellent is limited to the area or areas protected and by its duration Repellents may be used in liquid or in cream form, or the clothing may be impregnated The repellents available now are materials of low sensitivity index

University of Cincinnati

rare instances keloid,[1] melanoma,[2] severe pyogenic infection,[3] amputation,[3] gangrene[3] and even death[3] have been reported as direct consequences of tattooing

Allergic reactions to the material used in tattooing can occur immediately or at any time during the existence of the tattoo Allergic reactions to mercury, usually used in the red part of tattoos, have been most frequently noted[4] The allergic dermatitis may either be confined to the tattoo or be generalized The allergenic mercurial compound causing the dermatitis need not be the mercuric sulfide (cinnabar) in the tattoo, but it can be any form of mercury which is used on the skin or internally

Local or systemic disease can be injected into the skin at the time of the operation The manifestations of the injected disease may appear at once or later, the time depending on the particular characteristics of the disease Leprosy,[5] tuberculosis,[6] syphilis,[7] tetanus,[4f] erysipelas[8] and chancroid[8] are reported to have been contracted in this manner

1 Cipollaro, A C Keloid Following Removal of Tattoo Mark, Arch Dermat & Syph **36** 160 (July) 1937

2 Sharlit, H Melanoma Caused by Indelible Pencil, Arch Dermat & Syph **37** 301-306 (Feb) 1938

3 (*a*) Shie, M D A Study of Tattooing and Methods of Its Removal, J A M A **90** 94-99 (Jan 14) 1928 (*b*) Berchon, E Histoire medicale du tatouage, Paris, J B Bailliere & fils, 1869, Arch de med nav **11** 23, 107, 187, 294, 370 and 441, 1869

4 (*a*) Unna, P Quecksilberuberempfindlichkeit und Tatowierung, Arch f Dermat u Syph **160** 153-155, 1930 (*b*) Ballin, D B Cutaneous Hypersensitivity to Mercury from Tattooing Report of a Case, Arch Dermat & Syph **27** 292-294 (Feb) 1933 (*c*) Muller, O Ueber einen Fall von Hautgeschwulstbildungen auf dem Boden einer Tatowierung, Dermat Wchnschr **106** 6-8 (Jan 1) 1938 (*d*) Madden, J F Reactions in Tattoos, Arch Dermat & Syph **40** 256-262 (Aug) 1939 (*e*) Swinny, B Generalized Chronic Dermatitis Due to Tattoo Report of a Case, Ann Allergy **4** 295-296 (July-Aug) 1946 (*f*) Novy, F G, Jr Generalized Mercurial (Cinnabar) Reaction Following Tattooing, Arch Dermat & Syph **49** 172-173 (March) 1944 (*g*) Sulzberger, M B Tattoo Dermatitis (Sensitivity to Cinnabar?), ibid **36** 1265 (Dec) 1937 (*h*) Sulzberger, M B, Kanof, A, and Baer, R L Complications Following Tattooing Sensitization and Desensitization to Mercury, Report of a Case, U S Nav M Bull **43** 889-894 (Nov) 1944

5 (*a*) Abramson, P D Tattooing A Brief Review of Its History, Pathology and Methods of Removal, New Orleans M & S J **84** 191-195 (Sept) 1931 (*b*) Porritt, R J, and Olsen, R E Two Simultaneous Cases of Leprosy Developing in Tattoos, Am J Path **23** 805-817 (Sept) 1947

6 Abramson[5a] Gould, G M, and Pyle, W L Anomalies and Curiosities of Medicine, Philadelphia, W B Saunders, 1897, p 751 Collings, D W, and Murray, W Three Cases of Inoculation of Tuberculosis from Tattooing, Brit M J **1** 1200 (June 1) 1895

7 Novy[4f] Lacassagne, A Les tatouages Étude anthropologique et medico-legale, Paris, J-B Bailliere & fils, 1881, cited by Shie[3a] Maury, F F, and Dulles, C W Tattooing as Means of Communicating Syphilis An Investigation of Twenty-Two Cases Exposed to Inoculation with the Virus of Mucous Patches, in Fifteen of Which Syphilis Followed, Am J M Sc **75** 44-62 (Jan) 1878 Cheinisse, L Chancres syphilitiques multiples consecutifs au tatouage, Ann de dermat et syph **6** 1-5, 1895

8 Wilde, A G Vaccina Infected Tattoo Case Report, New Orleans M & S J **82** 385-386 (Dec) 1929

Clinical Notes

PROGRESSIVE DISSEMINATED COCCIDIOIDOMYCOSIS

WERNER W DUEMLING, M D
SAN DIEGO, CALIF

In 1892 Wernicke [1] and Posada [2] reported the first known case of coccidioidal granuloma Two years later Rixford [3] described the first case in the American literature At that time the causative agent was considered to be a protozoan, because of the resemblance of the indolent ulcers of the skin in this disease to those produced in animals by coccidia, the name of coccidioides was suggested for this agent In 1900 Ophuls [4] recognized and described the causative agent as a moldlike parasite which was readily cultured on various mediums It has been within the last decade that valley fever, the syndrome of influenza and erythema nodosum, has been attributed to coccidioides [5] This recognition of the primary infection has caused a considerable change in attitude toward the disease Coccidioidal infection, once considered a rarity when recognized only in the granulomatous stage, is now not uncommon, however, the extensive and unusual involvement in the following cases which came under our observation merits reporting in detail

REPORT OF CASES

CASE 1—A M R, a 32 year old Mexican Indian, entered the United States Naval Hospital, Treasure Island, San Francisco, on April 8, 1944, complaining of a painful right ankle and sores on his skin He was born in San Diego and prior to his enlistment in the Navy on Dec 13, 1943, had lived in San Diego county

On March 15, 1944, a nodule developed on his left forefinger and his right ankle became painful Several days later nodules appeared on the left cheek and on the right side of the forehead These nodules were at first small, reddish purple and smooth-surfaced but later became verrucous and elevated, with a purulent discharge

The physical examination revealed a small, thin man in no distress, with purulent verrucous nodules on the left forefinger, right side of the forehead and the left cheek (fig 1) There was widespread lymphadenopathy and a warm, tender, swollen right ankle The examination revealed no further abnormalities

1 Wernicke, R Ueber einen Protozoenbefund bei Mycosis fungoides(?), Centralbl f Bakt **12** 856, 1892

2 Posada, A Un nuevo caso de micosis fungoidea con psorospermias, An d Circ med argent **15** 585, 1892

3 Rixford, E A Case of Protozoic Dermatitis, Occidental M Times **8**.704, 1894 Rixford, E, and Gilchrist, T C Two Cases of Protozoan (Coccidioidal) Infection of the Skin and Other Organs, John Hopkins Hosp Rep **1** 209, 1896

4 Ophuls, W, and Moffitt, H C A New Mold (Formerly Described as a Protozoan Coccidioides Immitis Pyogenes), Philadelphia M J **5** 1471, 1900 Ophuls, W Further Observations on a Pathogenic Mold Formerly Described as a Protozoan, J Exper Med **6** 443 (Feb) 1905, Coccidioidal Granuloma, J A M A **45** 1291 (Oct 28) 1905

5 Dickson, E C Coccidioides Infection, Arch Int Med **59** 1920 (June) 1937, Valley Fever, California & West Med **47** 151 (Sept) 1937

The erythrocyte sedimentation rate was 30 mm per hour, and the white cell count was 7,750, with 6 per cent eosinophils The reaction in the coccidioidin skin test was positive Aspirated pus from fluctuant cervical lymph nodes contained the double-contoured highly refractive spores characteristic of coccidioidomycosis The early lesions became granulomatous, and new abscesses developed in the left knee, the left buttock, the left portion of the thorax and submental region The diagnosis was verified by culture, biopsy and guinea pig inoculation The lesions were treated by drainage and excision, and potassium iodide was given orally, with little or no improvement On May 5 the patient was given a course of penicillin extending over a seven day period and totalling 1,000,000 Oxford units, with no appreciable change Roentgenograms on August 23 revealed parenchymatous infiltration of the subclavian portion of the right lung and destruction of the bone of the left seventh rib, all previous roentgenograms had shown no abnormalities Treatment with coccidioidin vaccine, at first a stock supply and later an autogenous



Fig 1—*A*, noduloulcerative lesions of the face *B*, detail of lesion on left cheek, showing close resemblance to blastomycosis

vaccine, was started on July 18, 1944 and continued at two week intervals The patient continued to lose weight, became cachetic and debilitated and, on Jan 1, 1945, died

Abstract of Necropsy Protocol—Gross Findings Lungs The right pleural cavity contained 2,000 cc of pale yellow fluid flecked with fibrin The lower lobe of the right lung was atelectatic, while the apex revealed several small cavities from 1 to 5 mm in diameter, forming a honeycombed tissue surrounded by a solid white parenchyma These cavities were lined by a pale gray, granulating membrane No definite miliary or nodular granulomas were seen on gross inspection

The left pleural cavity was almost obliterated by fibrous adhesions The cut surface of the lung did not reveal any gross pathologic changes The tracheobronchial lymph nodes were enlarged up to 1 5 cm The cut section revealed extensive caseous and calcareocaseous destruction

The last group of reactions includes the appearance of local or systemic disease in tattoos after the tattoos have become a site of lowered resistance Brose[9] demonstrated that all portions of tattoos are more sensitive to blows, rubbing and external mechanical stimuli than is normal skin Belote[10] and others showed that tattoos alter the distribution of secondary syphilis The lesions were accentuated in and around tattoos except in the red (mercuric sulfide) portion, where the protective influence of the mercuric ion was greater than the effect of the foreign pigment in lowering the resistance of the area This paper records the first case known to me of chronic discoid lupus erythematosus occurring in a tattoo



Fig 3—Low power view of microscopic section taken from a lesion in the tattoo, showing histopathologic features in keeping with chronic discoid lupus erythematosus

REPORT OF A CASE

J C, aged 36, a white male truck driver, was tattooed on the lateral surface of the left arm in 1943 The tattoo healed after the initial reaction and showed no signs of irritation until November 1947 Then the red part of the tattoo began to itch and burn A dermatitis appeared in the red part of the tattoo in about a week. The patient stated that there was not any known cause for the symptoms

9 Brose Neue Tätowierungsphänomene, Dermat Wchnschr **84** 461-463 (April 2) 1927

10 Belote, G H Tattoo and Syphilis, Arch Dermat & Syph **18** 200-209 (Aug) 1928

Heart The pericardial sac was completely obliterated by firm, fibrous adhesions except for a linear pocket of thick pus along the left side of the heart Here the visceral and parietal layers were roughened by a thick, organizing, fibrinopurulent exudate which extended up over the base

Alimentary Tract The mesothelial surfaces of the mesentery and of the parietal wall were moderately studded with fine, white, glistening miliary lesions, of pinpoint

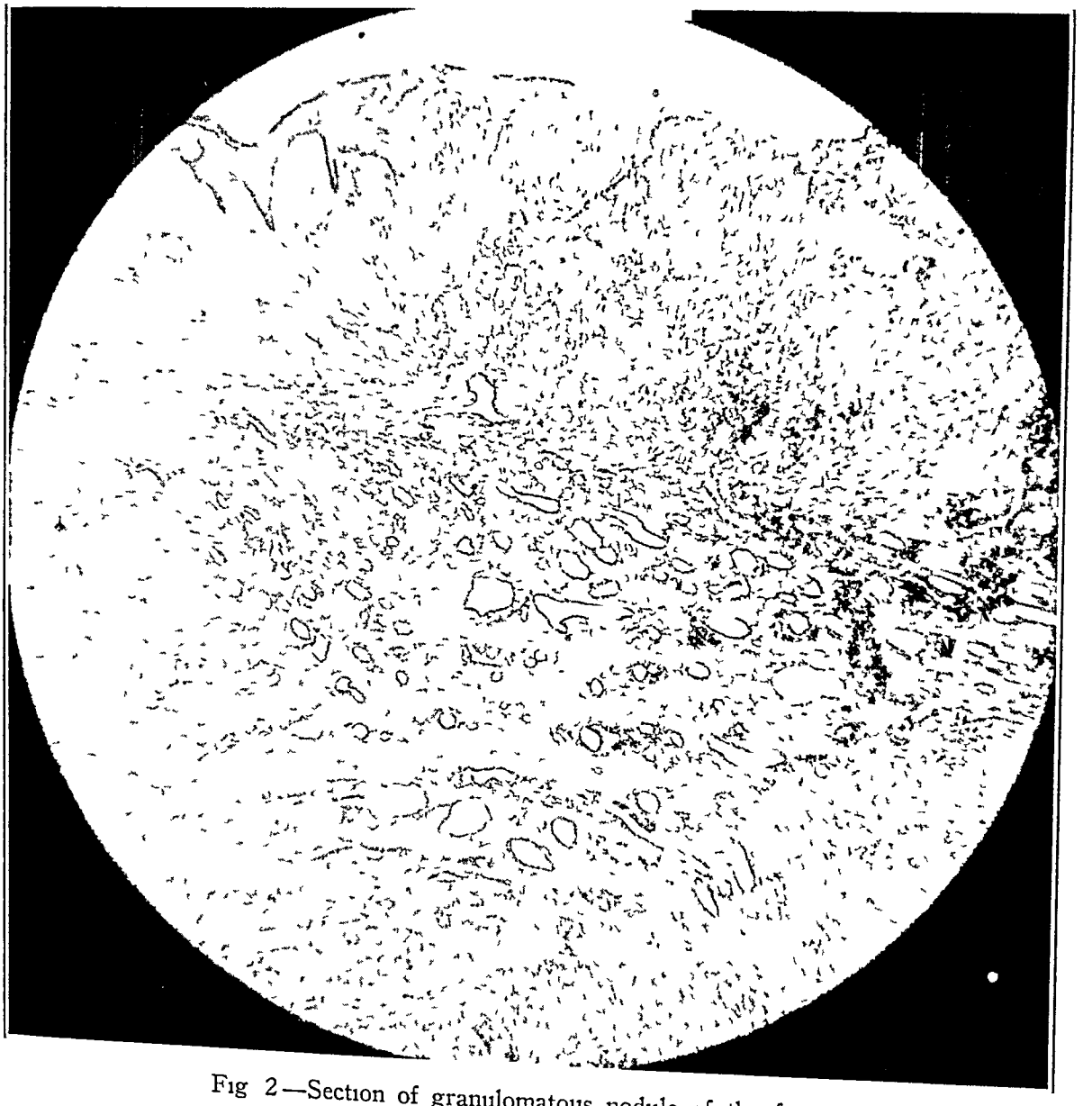


Fig 2—Section of granulomatous nodule of the face

to pinhead size Short fibrous tags were found along the mesenteric attachment and over the leaves of the mesentery

The esophagus was grossly normal except for a longitudinal lesion of 7 by 2 mm located on the anterior wall 7 5 cm below the rima glottidis The stomach had a pale pink and somewhat atrophic mucosa Three small, ulcerated outpouchings of the mucosa were located in the magenstrasse, 4 cm proximal to the pylorus These were about 3 to 4 mm in diameter, with smooth bases and borders The overlying serosa was thickened with fibrous tags The intestines

or the eruption This development was accompanied by a similar dermatitis on the face, which also itched and burned In March 1948 the patient had scattered, pea-sized to dime-sized, dry, round, erythematous, pruritic papules covered with an adherent carpet-tack-like scale on the face and in the red part of the tattoo There were about fifteen lesions on the face and four in the tattoo Reactions in the Mantoux test and in serologic tests for syphilis were negative A roentgenogram of the chest and other laboratory studies showed normal conditions Biopsy specimens from lesions on the face and from the tattoo showed histopathologic features which were in keeping with the diagnosis of chronic discoid lupus erythematosus All lesions seemed to respond to bismuth subsalicylate in oil given intramuscularly On two separate occasions the eruption showed an acute flare-up when the face was exposed to sun and wind for about three hours All lesions flared, even though those in the tattoo were protected by a shirt and a heavy leather jacket

SUMMARY

A case of chronic discoid lupus erythematosus with characteristic lesions on the face and in the red portion of a tattoo on the left arm is reported Wind burn and sunburn caused the eruption to flare simultaneously on the face and arm even though the eruption on the arm was protected by a shirt and heavy leather jacket

1228 Lowry Building

IDENTICAL ALOPECIA AREATA IN IDENTICAL TWINS

OWEN S HENDREN, M D
BIRMINGHAM, MICH

In the past many dermatologic and nondermatologic diseases have been reported in twins To enumerate only a few, they are lichen planus,[1] von Recklinghausen's disease (neurofibromatosis),[2] rosacea,[3] summer prurigo,[4] ichthyosis hystrix,[5] peptic ulcers,[6] calcified mesenteric glands,[7] pilonidal cysts,[8] ephelides,[9]

From the Department of Dermatology and Syphilology, Wayne University College of Medicine, Detroit, and City of Detroit Receiving Hospital, Dr Loren W Shaffer, Director

1 Epstein, S Lichen Planus Confined in the Oral Cavity in Twins, Arch Dermat & Syph **45**.382 (Feb) 1942

2 Loftis, E L Recklinghausen's Disease in Identical Twins, Arch Dermat & Syph **42** 657 (Oct) 1940

3 Saunders, T S Rosacea in Twins, Arch Dermat & Syph **50** 269 (Oct) 1944

4 Parkhurst, H J Summer Prurigo of Hutchinson in Twins, Arch Dermat & Syph **14** 625 (Nov) 1926

5 Gross, P Ichthyosis Hystrix in a Twin, Arch Dermat & Syph **35** 520 (March) 1937

6 Riecker, H H Peptic Ulcer in Identical Twins, Ann Int Med **24**·878 (May) 1946

7 Hoffstaedt, E G W Identical Disease in Identical Twins, Brit M J **1** 516 (April) 1945

(Footnotes continued on next page)

also contained similar small, shallow, ulcerated areas Their margins were formed by a delicate, pale, granular membrane, the overlying serosa was thickened by fibrous tags A solitary lesion was found in the duodenum, while about twenty-four such lesions were seen in the cecum and ascending colon Most of the lesions were 2 by 4 mm, with their long axes at right angles to the long axis of the bowel

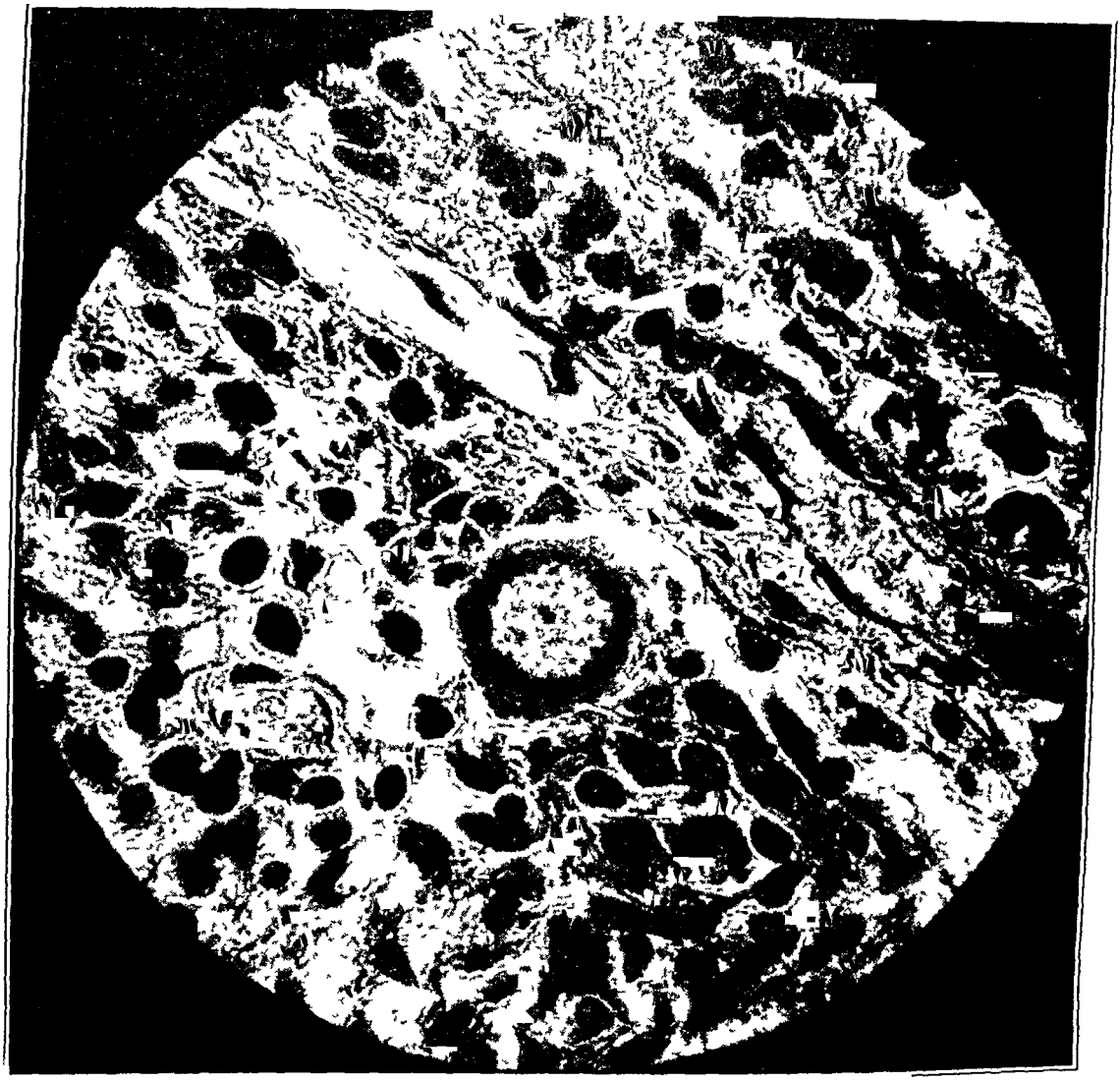


Fig 3—High power view, showing a characteristic mature endosporulating spherule

Osseous System The only significant bone lesion was a small area of osteomyelitis of the left seventh rib The cortex was irregularly thickened for a distance of 7 mm proximal to the medullary lesion on the pleural surface

Microscopic Observations (figs 2 and 3) In general the lesions were typical granulomas with numerous coccidioidal spherules The larger lesions showed tubercle formation, with central caseation The spherules were present free in the proliferating reactive border and within the Langhans giant cells The granulation tissue was composed of capillaries, proliferating endothelial cells and young collagen

lentigines,[9] and dermatitis herpetiformis.[9] There have also been reported several cases of allergy of similar type and onset.[10]

The following case of alopecia areata beginning at the same time on identical areas of the scalp in monozygotic twins aroused our interest

REPORT OF A CASE

Robert L. and Raymond L., 11 years of age, presented themselves to the Dermatology Clinic, City of Detroit Receiving Hospital, on Oct. 31, 1947, with the complaint that each had a bald spot on his head. Their mother stated that



Showing similarity in appearance of the twins and small areas of alopecia areata in identical locations on the right side of the occiput.

these spots had been first seen by her on the same day in June 1947, that to the best of her knowledge both had appeared at the same time and that she was sure that they had not been present the previous week.

8. Fox, P. F.: Pilonidal Cysts and Sinuses in Identical Twins, J. A. M. A. **125**: 120 (May 13) 1944.

9. Melsom, R.: Dermatological Investigations on Twenty-Two Pairs of Identical Twins, Acta dermat.-venereol. **25**: 29 (June) 1944.

10. Criep, L. H.: Allergy in Identical Twins: Report of Seven Pairs of Twins, J. Allergy **13**: 591 (Sept.) 1942.

connective tissue elements, a heavy infiltration of plasma cells and lymphocytes, tissue mast cells, mononuclear phagocytes with cell detritus and an occasional polymorphonuclear leukocyte Varying numbers and sizes of coccidioidal spores were scattered throughout this granulomatous tissue Many contained endospores, but in some instances they were devoid of these and appeared as empty cysts with double-contoured envelopes The cells of the tubercles were arranged in a

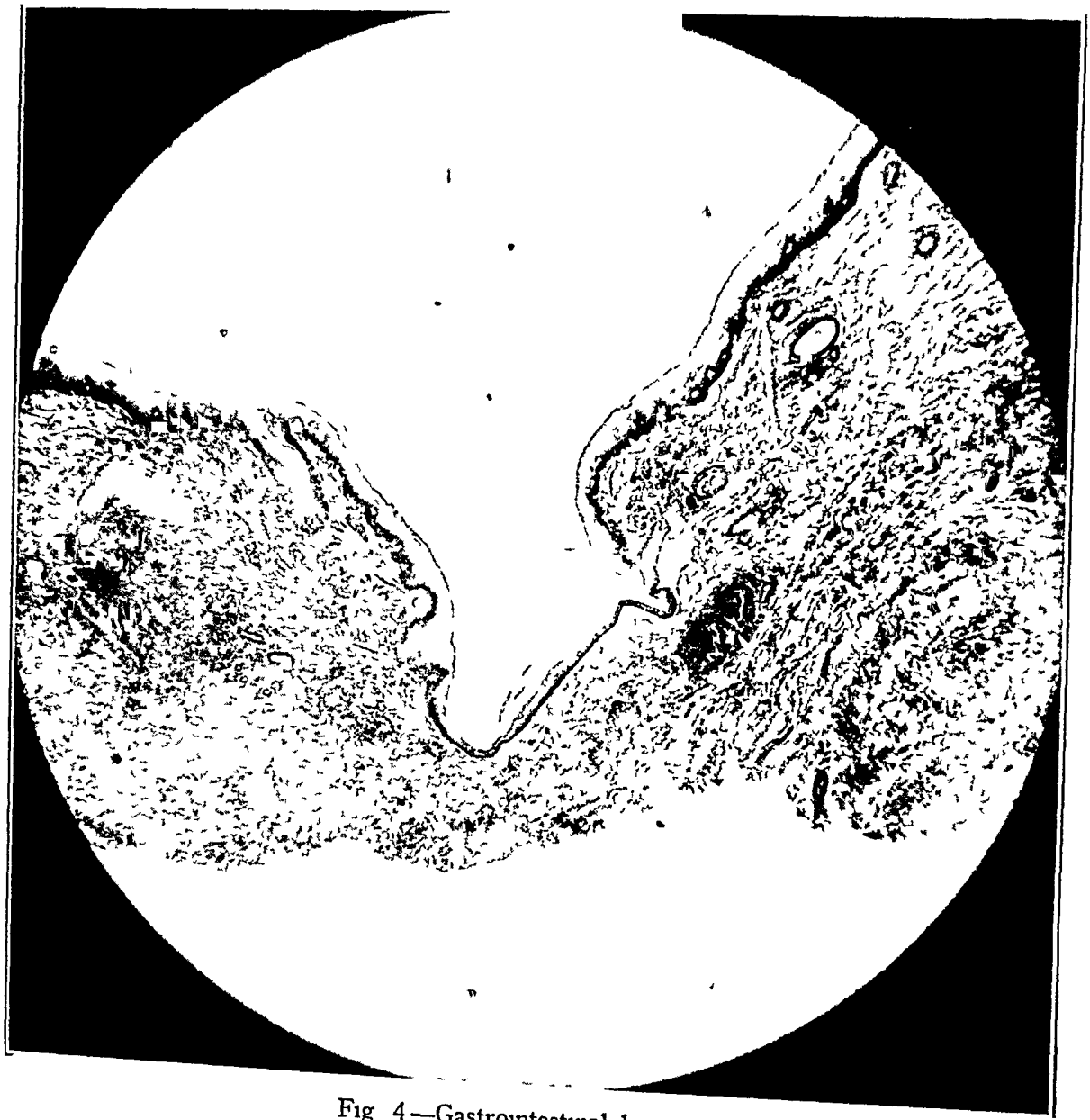


Fig 4—Gastrointestinal lesion

somewhat concentric, onionskin lamination The gastrointestinal lesions (fig 4) showed similar ulcerative granulomatous pathologic changes, involving the mucosa, submucosa and, to a lesser extent, the muscularis

Case 2—E A H, a 20 year old American Negro, was admitted to the surgical service of the United States Naval Hospital, San Diego, Calif, on Jan 26, 1946, complaining of pain in the right upper portion of the abdomen Prior to the completion of comprehensive laboratory examinations he constituted an interesting diagnostic problem, inasmuch as the differential diagnoses listed, among other

The family consisted of the mother, the father and 4 children No other member of the family had or ever had had a similar type of loss of hair Both patients had had measles and pertussis at 18 months of age Robert had had chickenpox when he was 6 years old, but Raymond had not There was no history of other previous illnesses

On examination the boys were strikingly similar in appearance, with the same shade of hair and with the same characteristics in regard to ears, teeth, nose and mouth In all zones of the iris of both patients there was the same type of pigmentation and distribution[11] Both boys exhibited a small area of typical alopecia areata in identical locations on the right side of the occiput approximately 2 by 0 75 cm Below each lesion there were three smaller areas of thinning of the hair but no complete loss in any place except those previously mentioned

Repeated examinations of the scalp under the Wood light revealed no fluorescence in the case of either boy Repeated cultures were negative for tinea capitis The hair appeared normal on direct microscopic examination Observations in blood counts (red cells, white cells and differential), as well as in urinalysis and serologic examinations, were all essentially normal

COMMENT

In a review of the literature for the past several years only 1 case of alopecia areata in twins was found,[12] and that case was somewhat different from the one here presented in that the lesions were not identical and did not appear simultaneously

Several theories have been advanced as to the cause of alopecia areata, but the exact etiology is unknown No single theory will account for all cases of the condition

In presenting this interesting and rather unusual case no attempt is being made to interpret the findings, and it is not our intention to try to prove or disprove any of the theories that have been advocated to date Rather, the case is presented purely as a dermatologic curiosity

1025 Pilgrim Road

11 Rife, D C Genetic Studies of Monozygotic Twins II Finger Patterns and Eye Color as Criteria of Monozygosity, J Hered **24** 407 (Oct) 1933

12 Turnacliffe, D D Alopecia Areata in Twins, Arch Dermat & Syph **24** 1122 (Dec) 1931

SUMMER PRURIGO

Report of a Case Controlled by Diphenhydramine (Benadryl®) Hydrochloride

HARRY W WOOLHANDLER, M D
PITTSBURGH

Summer prurigo is at best an incompletely understood entity While it is generally accepted that hypersensitivity to sunlight produces the eruption, the exact wavelength responsible has never been definitely established Experimental

From the Section of Dermatology, University of Pittsburgh School of Medicine

things, syphilitic hepatitis, subacute appendicitis, low grade hepatitis with multiple abscesses, parasitic infection of the intestine with perforation, trichinosis, secondary syphilis, nephrolithiasis, Loffler's syndrome, eosinophilic leukemia and pneumonitis

On January 24, epigastric pain, which lasted for about two hours, developed after meals On January 25, the patient had pain in the lower right anterior portion of the chest, but no dyspnea or infection of the upper respiratory tract, and afterward a persistent dull, aching pain appeared on the right side at the costal margin The following day, the patient first noticed two small papules, one on the midback and one over the epigastrium

The physical examination showed essentially normal conditions except for moderate tenderness in the right upper quadrant at the costal margin The abdomen was soft, and no masses or organs were palpable The chest appeared clear on auscultation and percussion Over the midepigastrium and midback there were two small, suppurating nodules



Fig 5 (case 2) —Showing lesions of lips and chin from which Coccidiodes immitis was isolated

The erythrocyte sedimentation rate was 18 mm per hour, and the white cell count was 11,250, with 24 per cent eosinophils Subsequent blood counts all revealed an eosinophil count averaging about 14 per cent Repeated coccidioidin skin tests had negative reactions Reactions to the Kahn and Kline tests were initially positive, but to the Kolmer, Wassermann and repeated Kahn tests they were negative Biopsy of the nodule over the upper portion of the abdomen revealed numerous double-contoured, highly refractive spores characteristic of Coccidioides immitis Roentgenograms of the chest showed increased mottled markings of the central and lower central lung fields

The patient was put on a supportive regimen but continued to have a low grade fever He acquired new cutaneous lesions (fig 5) similar to the original two and rapidly began to fail as the pulmonary infection progressed C immitis was isolated from the purulent discharge of the ulcerating lesions He was given whole blood transfusions, 100 cc of protein hydrolysates (parenamine®) daily and 15 drops of

reproduction of this dermatosis has been accomplished with ultraviolet rays, ordinary sunlight, sunlight passed through window glass, yellow and red rays of longer wavelength only and even alpha and gamma rays [1] Attempts at desensitization have generally been unsuccessful, and, except for symptomatic treatment and avoidance of sunlight, no therapeutic measure of merit has been described Thus, the dramatic response to diphenhydramine hydrochloride (benadryl hydrochloride®) in a recently treated patient appears worthy of reporting

REPORT OF CASE

A 5 year old white girl was first seen by me on April 9, 1947, with an eruption of the cheeks and nose of four days' duration History obtained from the mother indicated that the patient had previously had a similar eruption lasting from June 1946 to October 1946, which initially had involved the face and the forearms At that time the patient had been seen by the family physician, who had prescribed daily exposures to sunshine After a few days of such exposures the eruption spread to the arms, legs and chest, with the lesions becoming moist and crusted for the first time There was no response to local applications, but in early October the eruption healed spontaneously The child's skin then remained entirely clear until April 5, 1947, when the eruption reappeared

Examination on April 9 revealed an eruption involving the cheeks and the nose and consisting of grayish red plaques, which on closer inspection were seen to be made up of closely set papules with adherent scales The lesions on the nose were entirely discrete, while those on the cheeks had coalesced into small plaques A diagnosis of summer prurigo was made, and on April 17 the patient was presented before the Pittsburgh Dermatologic Society, where this diagnosis was accepted by all except one member, who stated the belief that the disease was a dry staphylococcic infection

On April 9, the date of the first visit, the patient's mother was admonished to keep her out of direct sunlight, and a paste containing 3 per cent ichthammol (ichthyol®) was prescribed However, the mother permitted the child out in the sunlight as usual, and three days later the eruption had spread to the forehead and forearms, the original areas of involvement on the cheeks and nose having become more extensive A bland paste containing menthol, phenol, boric acid, zinc oxide, petrolatum and rose water ointment was substituted for the ichthammol paste and elixir benadryl hydrochloride® (a preparation containing 0 25 Gm diphenhydramine hydrochloride [benadryl hydrochloride®] in an elixir containing alcohol, glycerin and water, with sugar, flavoring oils and added color, in each 100 cc) 1 fluidrachm (3 7 cc) three times daily, was prescribed On April 17 the eruption showed no appreciable change, but on April 24 there was striking improvement, the face being almost entirely clear and the eruption on the forearms improved When the patient was next seen, on May 8, the skin of the face was entirely normal and the eruption of the forearms was barely discernible On June 7 no evidence of the original eruption could be seen, but a small area of involvement was found in the sternal region The child's mother admitted having permitted the girl out in the sun during a recent hot spell with no clothing except bathing trunks A promise was then exacted that the child would at no time be permitted outside with less clothing than a dress The sternal involvement

1 Becker, S W, and Obermayer, M E Modern Dermatology and Syphilology, ed 2, Philadelphia, J B Lippincott Company, 1947, p 291

a saturated solution of potassium iodide three times daily On March 26, he was started on a course of penicillin, receiving 50,000 units every two hours for a total of 3,600,000 units His downward course progressed, and on April 2, just after completion of the course of penicillin, he began to exhibit signs and symptoms of cerebral involvement, which terminated in meningitis Spinal puncture revealed a grossly clear fluid which, on microscopic examination and later on culture, revealed C immitis On April 7, the patient died Postmortem examination revealed miliary coccidioidomycosis of the meninges, lungs, spleen and lymph nodes and a large granuloma of the sternum and the right second rib anteriorly There were many extradural abscesses The microscopic examination of all the tissues involved confirmed the gross findings, revealing typical lesions packed with C immitis

SYMPTOMATOLOGY AND CLINICAL COURSE

The infection assumes a wide variety of manifestations, ranging from the asymptomatic variety to the frequently fatal disseminated form, and can be best understood and discussed under the following classification proposed by Smith [6] Clinically it may be divided into three forms primary, intermediate and progressive

Primary Stage—In the majority of cases in the endemic areas, the onset of the initial infection may pass unrecognized or be interpreted as a mild infection of the respiratory tract This was probably the situation in 1 of our cases (case 2), in which the patient gave a history of an infection of the respiratory tract two months prior to his admission to the hospital On the other hand, the respiratory symptoms may be prostrating and more prolonged, accompanied by malaise, substernal pain in the chest, cough, night sweats and nasopharyngitis A small percentage of patients suffer a recurrence of fever in from three days to three weeks, associated with erythema nodosum or erythema multiforme, regarded as an expression of the allergic state While the disease in this stage is usually self limited, it must be remembered that a very small undetermined percentage may steadily progress to the disseminated form

Intermediate Stage—With a few exceptions the pathologic changes and symptoms in this stage are strikingly like those found in tuberculosis The findings may vary from the mildest to massive consolidation, cavity formation or scattered lesions resembling miliary tuberculosis, and the course may likewise vary in direct relation to the severity of the involvement Although cavity formation may occur without subjective symptoms, most patients complain of pleuritic pain and a productive cough Unlike the situation with tuberculosis, even patients with the most extensive pulmonary involvement recover, and the symptoms in relation to the amount of involvement are less severe than in tuberculosis Treatment is entirely symptomatic, with the elevation of the sedimentation rate the best guide for clinical management

Progressive or Disseminated Form—Fortunately the incidence of this form of the disease, which carries a very high mortality, is very low The incidence is definitely higher in the heavily pigmented races, of which both patients whose cases form the basis of this report were members The symptoms and the course vary with the organs involved, and the disease may terminate in death in a period of from a few weeks to a year In 1 of our cases the disease was more fulminating in type, terminating with meningitis in about two and one-half months, while in the other the patient lingered on for nine months Involvement of the bones, joints,

6 Smith, C E Coccidioidomycosis, M Clin North America **27** 790 (May) 1943

healed in a few days, and no further relapses occurred during the entire summer Use of diphenhydramine hydrochloride was stopped on October 15, and there was no recurrence of the eruption up to Feb 15, 1948

COMMENT

An attempt was made during the management of this case to obtain consent to temporary discontinue use of the diphenhydramine hydrochloride (benadryl hydrochloride®), in order more definitely to establish the role of this drug in treatment of summer prurigo The mother's refusal prevented this or any other experiments from being carried out Nevertheless, I feel that the evidence, while presumptive, indicates that diphenhydramine hydrochloride was responsible for the control of this eruption At no time was any other medicament, except the bland paste mentioned, employed and the child was apparently exposed to direct sunlight regularly during the entire spring and summer That the diagnosis was probably accurate is attested to by the almost unanimous agreement of more than twenty dermatologists Further use of this drug in treatment of summer prurigo is definitely indicated, similar results would, of course, suggest that histamine plays a role in the causation of summer prurigo

8122 Jenkins Arcade (22)

SOLID CARBON DIOXIDE AS AN ANESTHETIC IN ELECTRODESICCATION OF CUTANEOUS BLEMISHES

ALEXANDER BREGMAN, M D
Associate Dermatologist, Englewood Hospital, Englewood, N J
EDGEWATER, N J

The electrodesiccation of cutaneous blemishes necessitates the use of local anesthesia because without it the procedure is too painful to be acceptable to patients Of the two methods of producing local anesthesia, namely, ethyl chloride freezing spray and infiltration with procaine or similar drugs, the local infiltration anesthesia is the more practicable Ethyl chloride spray is impracticable for two reasons It is inflammable, and thus unsafe for use in the presence of a spark, and the anesthetic effect wears off by the time the ethyl chloride has evaporated In using electrodesiccation for such lesions as pigmented moles or common warts in the region of the cartilaginous portion of the nose it is sometimes difficult for one to employ an anesthetic acting by local infiltration because of the close proximity of the underlying cartilage and lack of loose subcutaneous tissue which would allow infiltration with the anesthetic

Solid carbon dioxide used for its anesthetic effects works well in such situations It possesses the advantages of other types of compounds producing local anesthesia without exhibiting their drawbacks, and is less objectionable to the patient It is not inflammable, and it is of more lasting effect than is ethyl chloride spray, the latter characteristic being accounted for by the fact that ethyl chloride produces a temperature of about —31 F, whereas with solid carbon dioxide a temperature as low as — 110 F can be obtained

Although any type of machine for making solid carbon dioxide can be used satisfactorily for this purpose, I employ the Kidde dry ice® apparatus The whole

lungs, mediastinum and lymph glands is common, with the frequent development of verrucous and granulomatous nodules of the skin and subcutaneous cold abscesses The development of meningitis is evidence of wide dissemination and may occur with or without extensive visceral involvement The course of the meningitis is not unlike that of tuberculous meningitis, and, coincident with mental confusion in 1 of our cases, spherules of C immitis were demonstrated in the spinal fluid Gastrointestinal involvement is said not to occur because of digestion of the spherules, but Greaves [7] reported lesions in the small intestine and Ruddock [8] made the diagnosis by peritoneoscopy in a patient thought to have tuberculous peritonitis One of our patients (case 1) presented multiple lesions of the gastrointestinal tract, extending from the esophagus to the transverse colon They consisted of small, ulcerated outpouchings of the mucosa, 3 to 4 mm in diameter, with smooth bases and borders The margins of the ulcers were formed by a delicate, pale, granular membrane, the overlying serosa was thickened by fibrous tags The long axis of most of the lesions was at right angles to the long axis of the bowel

Treatment.—We are not concerned with the treatment of primary or intermediate coccidioidomycosis in this paper Suffice it to say that bed rest and symptomatic therapy will eventuate ultimately in clinical recovery, except in those cases with extensive cavitation, in which pneumothorax is required It is the progressive variety, of which the cases herewith presented are examples, that have so far been unaffected by a wide choice of remedies The drugs which have been of some value in other deep-seated mycoses, such as thymol, iodides, copper and antimony compounds and potassium tartrate, have uniformly failed to influence the course of the disease Penicillin offered nothing in our hands and has been reported by others [9] as ineffective Great hopes have been entertained for vaccines, but both the use of a stock and autogenous vaccine over a long period of time in increasing doses has been of no avail In order to rid the patient of large reservoirs of organisms which would otherwise be disseminated, all accessible granulomatous nodules were removed Roentgen therapy has been of no benefit, except to flatten exuberant granulomas The outlook in the progressive form of the disease must still be regarded as hopeless

EPIDEMIOLOGY

The epidemiology of coccidioidomycosis has become increasingly important because of the large numbers of men from all parts of the country brought into the endemic areas for training purposes during the past war and because of definite evidence of spread of the endemic areas For a long time after its first recognition, cases were reported only in those living in or near the great central valley of California It was not until 1920 that the first case east of the Mississippi was reported, and in the next decade there were accounts of sporadic cases in the Middle West and the eastern states A recent study by Smith [6] now reveals endemic areas occupying the great central valley of California and extending into southern California, all of Arizona, southern Nevada and southern Utah, probably parts of Idaho, all of New Mexico, western Texas and at least northern Mexico

7 Greaves, F C Coccidioidal Granuloma with Lesions in the Small Intestine, U S Nav M Bull **32** 201 (April) 1934

8 Ruddock, J C, and Hope, R B Coccidioidal Peritonitis Diagnosis by Peritoneoscopy, J A M A **113** 2054 (Dec 2) 1939

9 Michael, P , McLaughlin, R F, and Cenac, P L Coccidioidomycosis Report of Unsuccessful Treatment with Penicillin, U S Nav M Bull **43** 122 (July) 1944

procedure of producing anesthesia by freezing does not take more than a couple of minutes I apply the solid carbon dioxide pencil for ten seconds with moderate pressure and then proceed with electrodesiccation

After having used this method on a few patients with lesions in the nasal region and having proved to my complete satisfaction its feasibility and practicability I began to employ it in producing anesthesia on other parts of the body whenever electrodesiccation was indicated—in treating small isolated lesions of various natures I submit this method in the expectation that others may try it to determine the possibilities of this simple and practical way of treating cutaneous blemishes

4 Dempsey Avenue

ALLERGY TO WAX CRAYONS

Report of a Case

MIRIAM LUTEN, M D
PORTLAND, ORE

In 1947, two reports of cases of poisoning by wax crayons appeared in the literature The first one, by Jones and Brieger,[1] described a child in whom symptoms of severe paranitraniline poisoning developed as a result of the patient's eating red and orange crayons In the second report, Clark [2] told of the case of a child who acquired methemoglobinemia from eating yellow and orange crayons Schwartz, Tulipan and Peck [3] stated that school teachers may acquire dermatitis of the terminal ends of the thumb and index fingers from the dye in colored crayons They found that among 81 workers in refineries manufacturing paraffin 19 had boils or acne on their arms and hands They found that oil and wax acne differs from acne vulgaris in that the eruption in oil and wax acne is oftener found on the body and legs than on the face, which situation they attributed to the plugging of the orifices of the hair and the sebaceous follicles, with formation of comedos which become secondarily infected They expressed the opinion that the percentage of wax warts, acne and pustules decreases in direct proportion to the purity of the paraffin handled and that workers handling the white, refined product are almost free from these conditions

REPORT OF CASE

S S D, a 7 year old girl, came to the office, complaining of sties which had been present almost continuously for four years For the previous two years she had had severe itching of the axillas and the buttocks, followed by many furuncles in these regions Treatment had consisted of stock and autogenous vaccines, stannoxyl® (a preparation containing 42 5 per cent metallic tin and 7 5 per cent tin oxide) and general hygienic measures, all without benefit There were no refractive errors

1 Jones, J A, and Brieger, H Poisoning Due to Ingestion of Wax Crayons Report of a Case, J Pediat **30** 422 (April) 1947

2 Clark, E R Poisoning Due to Ingestion of Wax Crayons Report of a Case, J A M A **135** 917 (Dec 6) 1947

3 Schwartz, L, Tulipan L, and Peck, S M Occupational Diseases of the Skin, ed 2, Philadelphia, Lea & Febiger, 1947, pp 240, 243 and 858

density visualized in the left apical region superimposed on the posterior border of the third left rib, with the suggestion of a drainage band extending to the left *hilus*

Histologic section revealed acanthosis with edema of the prickle cell layer The corium is edematous and contains a cellular infiltrate composed of lymphocytes, plasma cells and leukocytes Deep in the corium there are numerous double contour bodies with a few giant cells

DISCUSSION

DR. OLIVER S ORMSBY I had been practicing only about a year when I was called to see a patient who was supposed to have tuberculosis A man of middle age had lesions on the face and on the extremities The lesions on the face were fairly typical of blastomycosis, but the lesions on the extremities were very different In those areas there were subcutaneous nodules, abscesses and ulcers, with pus oozing out of the lesions I took a specimen to the office and demonstrated Blastomyces The patient was very ill and died shortly thereafter At autopsy I was able to demonstrate Blastomyces in the lungs, liver, spleen, kidneys and bones That was the first case on record in which there was systemic blastomycosis involving all the tissues

During the next three or four years I saw 4 or 5 more cases, and it was shown that this organism attacks every tissue in the body At autopsy the doctor in charge pricked his finger, and within a little while blastomycosis developed in that finger, and within two or three months he had systemic blastomycosis In our early experience practically 100 per cent of the patients died Since that time a certain percentage recover

DR M J REUTER, Milwaukee One of our residents checked over our records on systemic blastomycosis and was able to find 38 cases of the generalized type Of this number he was able to trace 26 One patient is still alive after ten years and another is alive after two years

Paraffinoma Presented by DR T CORNBLEET and (by invitation) DR D COHEN and DR J GRAFFIN

C H, a white woman aged 63, about twenty-five years ago, had wax injected into both cheeks and the forehead for cosmetic purposes At present she is in a medical ward at the Cook County Hospital with arteriosclerotic heart disease and possible endocrine disturbance Examination revealed a firm mass, 5 cm in diameter, in both cheeks, and a smaller one between the eyebrows The overlying skin is bound down to the masses and is bluish red

The Kahn reaction of the blood was negative The urine was normal The electrocardiogram reveals myocardial damage Histologic sections from the mass in the cheek are presented

DISCUSSION

DR OLIVER S ORMSBY I saw one of those cases in my early experience It was only the second case that had been seen in this country My co-workers and I were fortunate enough to get a section which showed the typical sievelike arrangement where the paraffin entered the connective tissue This woman was very handsome, and she decided to have some dimples put in each side and to have some wrinkles taken out A half dozen large tumors developed A plastic surgeon removed them, and the result was very good At a later date we saw tumors from paraffin oil used for injection

DR S J ZAKON There are a lot of Romansky injections being given in the treatment of syphilis and other diseases with penicillin in large doses I have seen

a number of severe reactions in the buttocks following such injections The reactions would subside in a couple of weeks I wonder whether fifteen or twenty years from now one will see lesions similar to paraffinoma due to Romansky injections

DR STEPHEN ROTHMAN With vegetable oil and fatty acids paraffinoma does not occur Paraffinoma occurs exclusively with hydrocarbons I doubt whether white wax would produce paraffinoma, because such wax is composed of fatty acid

DR THEODORE CORNBLEET It is my feeling that one need not expect the same accidents to happen from the Romansky formula as from paraffin itself With paraffinoma there is no initial reaction, whereas with white wax one commonly finds a reaction in the tissues Originally, I tried to arrange to have a fluorescent light to detect the presence of the paraffin, which shows a Swiss cheese structure

Sporotrichosis Involving the Face and All Extremities Presented by DR MICHAEL H EBERT and (by invitation) DR N L BAKER

Dermatomycosis (?) Localized to Flexural Areas for Twenty Years Presented by DR H RATTNER and (by invitation) DR H RODIN and DR N L BAKER

Acute Disseminated Lupus Erythematosus in a Man Aged 37 Years Presented by DR MICHAEL H EBERT and (by invitation) DR N L BAKER

A Case for Diagnosis (Eruption Due to Drugs? Hemorrhagic Lupus Erythematosus? Toxic Purpuric Disease of Undetermined Origin?) Presented by DR S ROTHMAN and (by invitation) DR L RUBIN

Keratosis Follicularis (Darier?), Improved After Ingestion of Butter in Large Quantities Presented (by invitation) by DR H H RODIN

Recurrent Alopecia Areata Presented by DR E M SMITH JR

D D, a white boy, aged 7, rather small for his age, has a recurrent patch of alopecia areata involving the vertex and the strip down the center of his scalp toward the front This condition has occurred every September or October for the past five years and has run a course of about two or three months The configuration of hair loss is practically the same, and there is a complete clearing up of the condition between times

DISCUSSION

DR STEPHEN ROTHMAN I thought that definitely the boy had trichotillomania and that he had done a good job for himself

DR E M RUSTEN, Minneapolis I have a patient who is a resident in a tuberculosis sanatorium In 1928 he had pulmonary tunberculosis with bilateral effusion and rather extensive alopecia areata The pulmonary tuberculosis was controlled by sanatorium treatment, and he had a recurrence of hair growth About a year ago he had a recurrence of the pulmonary disease and again had alopecia areata His pulmonary disease is now improving, and his hair has also returned

DR JAMES R WEBSTER When I first saw the patient this afternoon I had the impression that the condition was trichotillomania, but on further examination concluded it was alopecia areata

After the suggestion that this condition could be due to allergy, the mother could recall only one material that the child had used continuously during this time At 3 years of age, she had started playing with wax crayons every day Patch tests of wax crayons and fatty extracts of house dust and dog hair made on the skin around the axillas were indeterminate When crayons were taken away from the child, she was free from sties and boils for two and one half weeks, the longest period in the past four years She was given a crayon for two minutes Within one-half hour, her eyelids became red, and sties appeared on the lids by the next morning Perma® crayons, which the manufacturer stated are made by an entirely different process from that used in making the crayola,® produced sties after similar exposure During the succeeding months, infections on the lids followed the child's handling of pictures colored by other children and contact with candles Colored pencils, protected by wood covers, were tolerated for a short time only

Four trials were made with a piece of wax without dye, which was furnished by the manufacturer After one of these trials, a small sty appeared Smears made from the draining pustules contained diplococci The last trial with both uncolored and colored wax, one year later, caused only a generalized pruritus but no sties

The only local therapy used was tyrothrycin, which the mother believed shortened the duration of the lesions

Throughout the summer months, when the child was not in school or exposed to wax crayons, she remained free from cutaneous lesions, except for one episode in which a severe edema of the eyelids followed playing in weeds This edema disappeared almost at once when the child's face was washed Scratch tests at this time showed strong reactions to the pollen of English plantain

SUMMARY

A case is reported in which sties, furuncles and pruritus repeatedly followed exposure to wax crayons

919 Taylor Street Building (5)

Results of examination of the bone marrow obtained by puncture of the sternum were not diagnostic It showed a decreased cellularity (hypoplasia) with good myeloid distribution, moderate eosinophilia and normal megakaryocytes

During the three weeks' stay at the hospital the patient's condition has remained unchanged A consultation was held with the thoracic surgeon concerning the tumor in the left anterior mediastinum A tentative diagnosis of teratoma or echinococcus cyst was made and exploration advised

DISCUSSION

DR DAVID BLOOM This eruption resembles sarcoid as seen in white persons It would be of interest to study the effect of calciferol in this case

DR LOUIS CHARGIN What is the pathologic report in this case?

DR FRANK E CROSS Clinically the lesion in this case is sarcoid, in spite of the lack of confirmation on histologic study It is possible that the biopsy specimens were taken from nonspecific sites Another biopsy specimen should be taken from a characteristic lesion and examined by a dermatopathologist

DR MAX BERKOVSKY Three biopsy specimens were taken and examined by the general pathologist at the Metropolitan Hospital and Dr Hyman at the New York Post-Graduate Hospital At no time could one justify the diagnosis of sarcoid on histologic study The reaction to the tuberculin test (1 10,000) was negatives Roentgenograms of the bones showed no abnormalities Roentgenographic examination of the chest revealed a mass which the surgeon said was a dermoid cyst in the anteriomediastinal space

DR. PAUL GROSS What has been done to rule out tuberculosis?

DR MAX BERKOVSKY No tuberculoid tissue was found on histologic examination There is nothing to warrant a diagnosis of leprosy

NOTE—The mediastinal tumor was removed by operation, and the histologic examination revealed a thymoma Subsequent histologic studies of cutaneous nodules by Dr W Sachs showed characteristic observations of lymphatic leukemia

Reticulum Cell Sarcoma Presented by DR DAVID B BALLIN

M M, a man aged 44, was previously presented before the New York Dermatological Society on Feb 25, 1947, by Dr Fred Wise, with the following note Additional data, such as results of the pathologic study of the left epitrochlear lymph node excised, roentgenogram of the chest, general medical examination, sternal puncture and electroencephalogram will be reported later

The patient is presented to show the rapid regression after 1 skin unit of roentgen rays (450 r) and to report the results of laboratory studies A hemogram taken on February 20 showed 5,160,000 erythrocytes, 1 8 per cent hemoglobin and a color index of 1 05 There were no eosinophils The results of sternal puncture and examination of the lymph node excised from the left epitrochlear region were reported as normal

Examination on April 16 revealed considerable regression in the satellite lesions about five weeks after the biopsy specimen was taken, but there was no diminution in the size of the main growth On April 3 1 skin unit of roentgen rays filtered through 1 mm of aluminum (450 r) was applied to the main lesion and about

Society Transactions

BRONX DERMATOLOGICAL SOCIETY

Wilbert Sachs, M D, *President*

Henry Silver, M D, *Secretary*

Feb 20, 1947

Lymphoblastoma, Tumors on the Forehead and Postauricular Subcutaneous Nodules Presented by DR MAX B KAMPF

Granuloma Annulare of the Legs with Keratotic Lesions Presented by DR LOUIS CHARGIN

Purpura Annularis Telangiectodes? Radiodermatitis? Hemostasis Dermatitis? Presented by DR PAUL GROSS

E B, a white woman aged 54, has had recurrent ulcerations on the feet for the past ten years In 1940 she was admitted to the Hospital for Joint Diseases because of multiple ulcers After the ulcers had healed many atrophic areas were found on the skin of both feet On the periphery of the atrophic patches were many bright red purpuric papules and telangiectases The diagnosis of purpura Majocchi was considered at the time, but the patient did not return for further treatment In October 1946 she was again hospitalized At that time large ulcers were present below the external and internal malleoli and on the dorsum of the right big toe Small ulcerations were also present on the dorsal and lateral surfaces of several toes of the left foot In addition, she had a seborrheic dermatitis of the nasolabial folds and eyebrows

The prothrombin time was increased to 30 seconds, and there was secondary anemia On October 16 the sedimentation rate was 70 mm in 45 minutes, on October 28, 45 mm and on, November 7, 15 mm The cholesterol content of the blood was 319 mg per hundred cubic centimeters, of which 30 per cent was free cholesterol and 70 per cent esterified cholesterol The thrombocyte count was normal The result of a tourniquet test for capillary fragility was positive The result of the Peck test with moccasin venom was positive on the forearm, thigh and the affected area

Treatment consisted of complete bed rest, applications of wet dressings with acriflavine and later of nitrofurazone ointment The patient was given ascorbic acid, 500 mg a day, vitamin B complex, folic acid, ferrous sulfate, and menadione The ulcers healed rapidly, and the patient was permitted to leave the bed for about an hour a day After two days of this regimen there developed purpuric macules and dark red puncta around the atrophic scars Some of these lesions changed into small necrotic ulcers the size of a pinhead

Since Dec 26, 1946, the patient has been receiving biweekly injections of moccasin snake venom No purpuric lesions have appeared recently, but there developed a small ulcer at the base of the left big toe

2 inches (5 cm) beyond When the patient was seen on April 15 the growth was entirely flattened out, so that it was only slightly elevated above the surrounding skin

Lichen Planus, Lichen Nitidus Presented by DR JOSEPH L MORSE

R S, a boy aged 7 years, was first seen at the Hospital for Joint Diseases with a generalized fine branny desquamation The mother stated that about three weeks previously the child had a generalized rash accompanied with fever A diagnosis of postscarlatinal exfoliation was made Urinalysis at that time showed a faint trace of albumin

The patient returned to the clinic in July 1946 presenting a number of discrete, somewhat lichenified patches around both ankles Under treatment with bland ointments the condition improved over a period of two months

In March 1947 the patient again visited the clinic At this time he had an eruption on the ankles, elbows, knees and dorsa of the fingers (terminal phalanges) On the ankles there were areas made up of violaceous shiny papules, on the elbows and knees there were many small flesh-colored papules, some in linear arrangement along scratch marks (Koebner phenomenon) There were no lesions on the trunk or genitals A diagnosis of lichen planus and possible lichen nitidus was made

A specimen taken from a lesion of the right elbow showed the epidermis to be covered by a thin keratin layer The basal cells were heavily pigmented At one point, just beneath the epidermis, there was a localized collection of inflammatory cells, including mononuclear cells and polymorphonuclear leukocytes The epidermis overlying this nodule of inflammatory cells appeared somewhat compressed and thinned out The histologic picture was consistent with a diagnosis of lichen nitidus A roentgenogram of the chest showed no abnormalities Results of quantitative tuberculin (human and bovine) tests in dilution of 1 10,000 and 1 100,000 were negative Kahn and Kline reactions of the blood were negative The urine was normal

DISCUSSION

DR MAX JESSNER The question of the occurrence of lichen planus and lichen nitidus simultaneously is an old one The patient shows definite lichen planus on the ankles, the lesions on the arms resemble lichen nitidus At the outset the lesions look almost alike There have been cases reported in which the two types have been found together One should, however, have histologic evidence in order to corroborate both diagnoses I think that the picture in this case fits in with the lichen planus type, especially in view of the lesions on the ankle

DR PAUL GROSS The case is of interest because of the rare association of lichen planus and lichen nitidus The tissue was somewhat damaged in the preparation for histologic examination, and, therefore, a definite diagnosis of lichen nitidus could not be made The typical tubercle-like structure was lacking, but it may be that even in lichen nitidus a nonspecific granuloma is present in the early stage of the lesion

DR WILBERT SACHS Conclusions cannot be drawn from this slide I agree with the diagnoses of lichen planus and lichen nitidus I have seen 2 similar cases

DR JOSEPH L MORSE As Dr Gross pointed out, this case was presented because of the rare association of the two diseases The lesions around the ankles were certainly characteristic of lichen planus An effort will be made to obtain biopsy specimens from both types of lesions

DISCUSSION

DR CHARLES WOLF I could not see any clinical manifestations of Majocchi's disease There is, however, a vasocirculatory disturbance present which produced sclerosis of the peripheral vessels I think that the pulsation in the dorsalis pedis is, if not entirely obliterated, at least decreased The atrophic changes are due to the sclerosis of the peripheral blood vessels

DR DAVID BLOOM Clinically the eruption resembles radiodermatitis No other diagnosis can be made from the appearance of the lesions tonight

DR MAX JESSNER I would be more inclined to regard this case as one of radiodermatitis, especially in view of the fact that ten roentgen ray treatments had been given to the area Moreover, the lesions suggest healed ulcers, perhaps with superimposed radiodermatitis The patient also presents a peculiar thickening of the skin of both knees, with yellowish discoloration, not unlike housewife's knee, which I do not remember ever having seen previously However, the usual keratosis in housewive's knee is missing here

DR LOUIS CHARGIN I agree with those who are of the opinion that this is not Majocchi's disease In Majocchi's disease the lesions are much smaller, situated higher up on the legs, usually there is some atrophy in the center, and the lesions are annular I cannot classify this process, but these scleroderma-like changes are not infrequently seen in elderly persons, particularly women

DR ERNST NATHAN The patient presents atrophic patches on the knees and on the legs, linear stripes along the tibias and scleroderma-like changes, all of which impressed me as acrodermatitis chronica atrophicans with scleroderma-like changes

DR WILBERT SACHS I do not consider radiodermatitis or scleroderma in this case Clinically, Majocchi's disease must be distinguished from Schamberg's disease and similar processes However, since Majocchi's presents a definite histologic picture, a biopsy would settle the diagnosis

DR PAUL GROSS As Dr Wolf stated, the cutaneous condition of this patient can be explained only by a vascular disturbance which leads to sclerosis of the peripheral blood vessels and atrophy of the skin The pathologic process accounts for the clinical manifestations consisting of telangiectasis, purpura, necrosis and atrophy This could be clearly followed by prolonged observation of the patient while she was in the hospital

The unusual feature of this case was the extensive ulceration which developed on the dorsa of the feet Because of this, it was difficult to consider the diagnosis of Majocchi's purpura unless there was something in the pathologic changes of the disease which could explain the atypical manifestations Actually necrosis has been described as part of the histologic picture of purpura annularis Apparently the severity of the vascular damage in this case produced sufficient necrosis to lead to ulceration Secondary infection may have been an added feature and has aggravated the formation of ulcers The improvement of the circulation by treatment with bed rest and antiseptic ointment brought about healing of the ulcers in a relatively short time If the ulcerations had been the result of a chronic radiodermatitis, the patient would have experienced severe pain, and healing would not have been prompt Prior to the patient's admission to the hospital, the case had been managed as a case of radiodermatitis without benefit

Dermatitis Herpetiformis Arsenical Keratoses and Pigmentation. Ulcer of the Leg Presented by DR ALEXANDER A FISHER

Tinea Glabrosa, Dermatophytosis, Onychomycosis, Pityriasis Versicolor, Erythrasma and Tinea Versicolor Appearing in the Same Patient Presented by DR EMANUEL MUSKATBLIT and (by invitation) DR L TULIPAN

The patient, a white man aged 65, has been seen at the Clinic of the New York University presenting several types of fungous infection 1 On both cheeks, especially the left one, in front of the ears, there is a faint erythema and scaling of about three weeks' duration Scrapings showed fungi of the ringworm type 2 On the neck there is a faint erythema, scaling and hyperpigmentation of a few weeks' duration 3 The upper middle part of the chest shows erythema, scaling, hyperpigmentation and some lichenification of about two months' duration Scrapings from the left side of the neck and chest showed fungi of the ringworm type 4 On the back there is a brownish scaly patch with numerous brownish macules on the periphery The duration is unknown Examination of the scales showed Malassezia furfur 5 On the left thigh there is a brownish-reddish patch with slight scaling and small foci on the periphery, of ten years' duration Scales from the thigh showed Actinomyces minutissimus and M furfur 6 The soles and lateral aspects of the feet showed scaling The toes and webs showed scaling and maceration of ten years' duration The toe nails showed yellowish and grayish patches and dulness Scrapings from the feet, toes and right big toe nail showed fungi of the ringworm type Cultures were planted with material obtained from areas infected with ringworm

NOTE—The toes showed Trichophyton purpureum All other culture tubes failed to show pathogenic fungi

Pseudopelade (Brocq) (Lupus Erythematosus?) in a Woman Aged 47 Presented by DR ELLEN REINER

Alopecia Cicatrisata (Pseudopelade) in a Negro Woman Aged 38 Presented by DR. LEO SPIEGEL and (by invitation) DR A KORNBLEET

A Case for Diagnosis (Cylindroma? Nevus? Papilliferus Syringadenomatosus? Turban Tumor?) Presented by DR CHARLES WOLF

Charles Wolf, M D, *President*

Henry Silver, M D, *Secretary*

Oct 23, 1947

Mycosis Fungoides, Fungoid Stage, Treated with Antimony Preparations Presented by DR JOHN GARB

D N, a woman aged 49, was registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Jan 17, 1940, presenting lesions of two years' duration The eruption began on the left thigh with a red, nonitchy, oblong patch about 3 inches (8 cm) in diameter Several months later oozing vesicular and crusted patches appeared on the chest and, shortly after, on the neck On the trunk the patches were erythematous and covered with silvery scales and showed minute bleeding points At that time a diagnosis of psoriasis vulgaris was made

On Jan 7, 1942, the microscopic examination of a specimen taken from the left elbow showed chronic eczema

Senile Elastosis of the Neck (Pseudo Xanthoma Elasticum?) Presented by DR PAUL GROSS

A Case for Diagnosis (Necrobiosis Lipoidica? Tuberculoderm?) Presented by DR MORRIS LEIDER and (by invitation) CAPT CHARLES D BELL

Ragweed Dermatitis Presented by DR ALEXANDER A FISHER

P B, a man aged 64, was in good health and free from any cutaneous disease until September 1936, when he walked barefoot through some lots in Astoria, N Y A vesicular eruption appeared on the back of the feet and legs It was diagnosed as dermatitis due to poison ivy and persisted for five months

The eruption recurred in September 1937, affecting mildly the feet, legs, face, hands, forearms and scrotum It then became perennial, with exacerbations from September to May The most comfortable months were June and July

At present there are thickened lichenified lesions on the face and forearms On the face the eruption is sharply limited to the upper part of the forehead

Patch tests with the following oleoresins gave positive reactions short ragweed, cocklebur, sheep sorrel, Kentucky blue grass, red top, short poison ivy, orchard grass and timothy Patch tests with protein extracts of trees, grasses and weeds showed a positive reaction only to oak Results of scratch tests with these protein extracts were negative The result of a patch test with a 5 per cent glycerine solution of ragweed oil (Hollister-Steer) was negative The patient has received oral treatment with oleoresins according to the Shelmire method

DISCUSSION

DR RUDOLF L BAER The patient had a positive reaction to the so-called "protein" fraction of the oak pollen I do not know whether there is any evidence that the oak protein has been of clinical significance Among the extracts available for testing, the "protein" fraction of oak pollen was included Unfortunately, no acetone extract of oak was available, so that it is impossible to state whether this patient is also sensitive to the oil fraction

It is probable that the fractions contained in various extracts differ considerably A patient suffering from a similar eruption at the New York Skin and Cancer Unit was tested with the following ragweed extracts (*a*) the oleoresin, (*b*) the so-called "protein" fraction in a glycerinated extract and (*c*) the so-called "protein" fraction in a powdered extract This patient reacted to the oleoresin fraction and to the powdered "protein" extract but not to the glycerinated extract, which is supposed to contain the same fraction as the powdered extract This indicates that there is a great difference between preparations which, it is assumed, contain the same fraction

DR CHARLES WOLF The history indicates that this patient was exposed to various flowers and pollens a long time ago, but not recently Still he exhibits a fairly pronounced eruption on the face and forearms, although he has not been in contact with these suspected allergens How can one explain the fact that the dermatitis still persists? Is it possible that this patient's sensitivity is polyvalent and reacts to many agents? What is the therapeutic approach to this problem?

The patient was readmitted to the New York Post-Graduate Hospital on Jan 8, 1943 At that time she presented a generalized erythematosquamous eruption The lesions were sharply marginated, of various sizes and round or oval, and they formed bizarre patches by confluence Most of them were elevated above the level of the surrounding integument and were edematous and infiltrated

In February 1943 a section of a specimen taken from the left forearm was examined histologically by Dr C F Sims The epidermis showed moderate and somewhat irregular acanthosis, with areas of parakeratosis alternating with retained granular layer Moderate intercellular edema and cellular infiltration were visible In the upper part of the corium were numerous small dilated vessels with edematous and thickened walls surrounded by moderate cellular infiltration of a polymorphous character Small round connective tissue cells, epithelioid cells, histiocytes and plasma cells were present In the zone of infiltration there was moderate interstitial and parenchymatous edema The histologic diagnosis was mycosis fungoides

The hemogram was normal, and the eosinophil count, 5 per cent The Wassermann reaction of the blood was negative The sedimentation rate was 10 mm per hour (normal in women, 19 mm per hour), as determined by the Westergren method Tests with old tuberculin elicited negative reactions in dilutions down to 1 5,000 and a plus-minus reaction in a dilution of 1 1,000 The icteric index was normal Roentgenograms of the chest revealed isolated old, calcified, central and parenchymal tubercle scars

During the seven years of observation the therapeutic measures included adequate courses of superficial fractional roentgen radiation exposures, courses of ultraviolet irradiation, and the administration of testosterone, oxophenarsine hydrochloride (mapharsen®) calciferol (vitamin D_2), promin® (sodium p,p'-diaminodiphenylsulfone-N,N'-didextrose sulfonate) intravenously and locally, bismuth subsalicylate, ethyl chaulmoograte, diphtheria toxoid, sodium arsenate, resin of podophyllum, riboflavin, ascorbic acid and anterior pituitary extract

During these years the patient showed no spontaneous remission of any of the lesions There was some temporary regression due to the roentgen irradiation or to some of the other therapeutic agents There was a tendency for most of the lesions to recur in a more aggravated form, and new lesions continued to develop

On April 28, 1947, treatment with antimony potassium tartrate was instituted On May 19, 1947, after ten intravenous injections of 5 cc of a 1 per cent solution of antimony potassium tartrate, given three times weekly, there was spectacular improvement The superficial patches were rapidly undergoing involution, and the raised growths were flattening out

From June 4 to August 8, because of possible toxic reactions, the treatment was changed to triweekly intramuscular injections of stibanose® (the diethylamino ethanol salt of sodium antimony gluconate), 4 cc per dose, the compound being a pentavalent antimony preparation containing 20 mg of antimony per cubic centimeter A total of nineteen injections was given On August 6, the patient was about 80 per cent improved

Electrocardiograms were taken every two to four weeks On August 11 minimal myocardial changes were observed Treatment with stibanose® was discontinued and crude liver extract and thiamine hydrochloride were given

On October 4 the electrocardiogram did not reveal any abnormalities of the ventricular complexes Injections of stibanose® were resumed twice weekly, alternating with administration of liver and thiamine hydrochloride

DR MARION B SULZBERGER In the preparation of plant extracts with the usual variety of solvents, one extracts a great number of different substances in each of the fractions Dr Coca and I have demonstrated that in the case of allergic contact dermatitis to ragweed and to certain other plants it was a fat-solvent soluble fraction which contained the usual allergen This might be misinterpreted The fact is that in most common forms of allergic eczematous contact dermatitis, water-soluble materials, including many dyes, metallic salts and local anesthetics, are responsible

DR ALEXANDER A FISHER This case is puzzling Some are of the opinion that the oil remains in wearing apparel for many months There is also, as Dr Wolf suggests, a possibility that this patient became allergic to pyrethrum, which is related chemically, and that is what causes the eruption to become perennial As Dr Sulzberger pointed out, the aqueous fraction is frequently responsible for the dermatitis The Mitchells have reported a case of the disease due to aqueous fraction of timothy which they were able to cure by injections of the ordinary extract used for hay fever

Angioma Resembling Idiopathic Multiple Hemorrhagic Sarcoma Presented by DR HARRY B FEILER

Wilbert Sachs, M D, *President*
Henry Silver, M D, *Secretary*
March 20, 1947

Erythroplasia (Cured by Application of a Mixture of Neoarsphenamine, Glycerin and Water) Presented by DR WILBERT SACHS and DR PERRY M SACHS

Erythroplasia of Queyrat (No Biopsy) Presented by DR CHARLES PINES

Poikiloderma Vasculare Atrophicans (Jacobi) Presented by DR FRANCES PASCHER

Pityriasis Rubra Pilaris Presented by DR DAVID BLOOM

F C, a woman aged 57, registered at the Skin and Cancer Unit of the New York Post-Graduate Hospital on Feb 14, 1947, complaining of an eruption of five weeks' duration The past and family histories were irrelevant

The patient presents on the face erythematous scaly plaques which toward the neck are associated with spinulous follicular keratotic plugs On the anterior and posterior aspects of the trunk there are irregularly shaped, erythematous scaly patches and groups of keratotic follicular yellowish or skin-colored papules or plugs the size of a pinpoint or pinhead On the extensor surfaces of the forearms and hands, lateral aspects of the arms and thighs, there is a similar eruption The scalp shows diffuse scaling On the forehead and around the eyes there are numerous small fibromatous lesions and skin tags The palms and soles show considerable brownish-yellowish hyperkeratosis

The patient has no subjective complaints and seems to be otherwise in good health

Examination on October 17 showed that all lesions, except for an isolated few, had completely regressed, leaving faintly superficial, reddish to purplish spots and dark brown patches The breasts, except for two small superficial patches, were entirely clear, the foul-smelling, crusted patches were replaced by normal epidermis A nodular growth on the middle of the left leg remained unchanged

DISCUSSION

DR FRANK E CROSS I should like to ask Dr Garb for the rationale of the use of antimony salts in the treatment of mycosis fungoides

DR JOHN GARB During the past five years I have experimented with many forms of treatment in mycosis fungoides, including promin,® testosterone propionate, diphtheria toxoid, chaulmoogra oil and many others The effect of these measures was only partial and temporary The use of antimony salts was purely experimental, prompted by the success obtained with them in treatment of granuloma inguinale The rapid melting of the ulcerated growth in mycosis fungoides (50 per cent improvement within three weeks) exceeded my expectation

DR CHARLES F SIMS I have examined several sections of specimens obtained in this case One of them presented a pleomorphic cellular infiltration in the upper part of the corium, as well as other histologic changes consistent with the diagnosis of mycosis fungoides

DR SAMUEL M PECK If this is truly a case of mycosis fungoides—and I value Dr Sims' opinion—then the treatment with antimony salts would rank as one of the important contributions to modern therapy It is well known that mycosis fungoides is a type of lymphoblastoma I hesitate to admit that the lymphoblastomatous type of lesion would respond to such a therapeutic measure If the antimony salts really have a beneficial effect on mycosis fungoides, it would be necessary for this disease to be removed from the group of lymphoblastomas I do not believe, however, that antimony salts would have such a beneficial effect on malignant lesions I have treated a variety of dermatoses, principally psoriasis, with antimony salts and have seen such cases clear up after one treatment However, recurrent lesions are resistant to antimony Further trial with antimony salts in treatment of mycosis fungoides is certainly indicated

DR BORRIS A KORNBLITH (by invitation) I have had much experience with antimony compounds, especially in the treatment of granuloma inguinale I have employed antimony potassium tartrate, stibophen (fuadin®), antimony sodium thioglycollate and stibanose® Since granuloma inguinale is a chronic disease and requires a prolonged period of therapy, a number of pertinent observations were possible in evaluating these antimony preparations

It is possible for one to give any of the antimony preparations up to a point of toxicity and to continue with a subtoxic dose for long periods because of the rapid excretion of these compounds through the kidney (for the most part, 80 per cent in twenty-four to forty-eight hours) and through the bowel (10 per cent) For cases requiring larger dosage for maximum therapeutic effect, stibanose® is by far the most advantageous drug There is no pain associated with its subcutaneous or intramuscular administration, while the other antimony preparations, such as antimony potassium tartrate, stibophen and antimony sodium thioglycollate, produce pain when given intramuscularly In general, it may be stated that larger doses of antimony are not possible because of the toxicity of the drug When a less toxic drug is introduced, the larger doses are well tolerated and a better

Results of laboratory examinations, including urinalysis, a Wassermann test of the blood and a determination of the vitamin A content of the blood, were normal The blood cell and differential count showed an abnormal low white cell count of 3,500 and relative lymphocytosis (56 per cent lymphocytes) The report of the histologic examination of an erythematous lesion taken from the abdomen was possible early exudative lichenoid discoid dermatosis

DISCUSSION

DR WILBERT SACHS Microscopically there is no evidence of this disease The picture is that of exudative discoid and lichenoid dermatosis Recently Dr Perry Sachs and I reported 3 cases occurring in female patients (*J Invest Dermat 8 215, 1947*)

DR PAUL GROSS I agree with Dr Bloom that this is a case of pityriasis rubra pilaris The patient has leukopenia, it would also be of interest to make a complete hemogram I recommend treatment with crude liver extract and folic acid

DR DAVID BLOOM I presented this case because it is clinically typical, and yet the results of the histologic examination did not confirm the diagnosis It should be noted that when the biopsy specimen is taken from an erythematous plaque in which the keratotic papules have disappeared the pathologist is unable to make a diagnosis of pityriasis rubra pilaris I wish also to mention that a majority of the patients with pityriasis rubra pilaris that I have observed were all in the fifth decade and not young persons as mentioned in dermatologic textbooks

DR PAUL GROSS O'Leary makes a distinction between pityriasis rubra pilaris and pityriasis-rubra-like eruptions I think that this division is justified by the clinical picture, course and response to therapy I cannot agree with Dr Bloom concerning the age groups involved I have seen several children with extensive eruptions, usually with a sudden onset, showing the clinical features of pityriasis rubra pilaris These patients have shown a dramatic response to a combination of vitamin B complex and vitamin A

Early Mycosis Fungoides, Psoriasiform Lesions Presented by DR ADOLPH ROSTENBERG and DR WILLIAM M SISKIND

Idiopathic Onycholysis, Improved with Thyroid and Vitamin A Therapy Presented by DR ALEXANDER A FISHER

V C, aged 16, first noticed about three years previously that the nails became soft and separated from the nail bed

When first seen, on Dec 17, 1945, all finger nails were involved (kodachrome® slide presentation) He had been under the care of another dermatologist for one and one-half years and had received roentgen ray treatment, ultraviolet rays and various ointments without apparent effect

Results of the physical examination were normal except for a pulse rate of 82 A medical consultant stated that at this age basal metabolism readings are not reliable, and the basal metabolic rate was therefore not established The patient was given thyroid, ¼ grain (16 mg) three times a day

When he returned in a week the pulse rate was 92, and he complained of nervousness The dose of thyroid was then reduced to ¼ grain twice daily, and he was given, in addition, vitamin A, 100,000 units daily, to augment the

therapeutic result obtained Initial resistance to antimony, however, is not overcome by increasing the dose

The immediate toxic reactions, in the order of their appearance, are as follows hacking cough, circumoral pallor, blanching of the face, respiration, nausea, retching, vomiting and vasomotor collapse All these symptoms are ameliorated by the prompt use of epinephrine subcutaneously (8 to 10 mm of a 1 1,000 solution) The late symptoms of toxicity are myalgia, especially of the deltoid and the quadriceps femoris muscles, pain along the distribution of the trigeminal nerve, especially in decayed teeth, and cardiac irregularities, such as bradycardia and auricular fibrillation, with occasional electrocardiographic changes

All observations were made on ambulatory patients, who tolerated the antimony drugs in a surprisingly asymptomatic way despite the large doses used

DR JOHN GARB I am in accord with Dr Peck If treatment with antimony preparations should prove effective in other cases of mycosis fungoides, then mycosis fungoides should be taken out of the group of lymphoblastomas

Similar remedies, such as chaulmoogra oil, are sometimes used in the treatment of leprosy and of mycosis fungoides It is interesting to note that antimony salts, alone or in combination with arsenic, have been used in the treatment of leprosy, with varying degrees of success, by Kingsbury and others (A New Antimony Compound in the Treatment of Leprosy, ARCH DERMAT & SYPH **24** 1053 [Dec] 1931)

As Dr Kornblith pointed out, the pentavalent antimony preparation stibanose® is the least toxic of all antimony products Nevertheless, toxic reaction, especially myocardial damage, must be guarded against

Keratosis Follicularis (Darier's Disease) Presented by DR NATHAN SOBEL

D N, a girl aged 14, presents an eruption which has been present for seven years, but which has become aggravated in the past four years The patient has no brothers or sisters The mother, father and other relatives are not affected by the disease

In both supraclavicular regions and on the sides of the neck there are areas of erythema the size of a palm, with extensive oozing and yellowish crusting The scalp and upper part of the forehead show similar areas There are numerous discrete keratotic lesions the size of a pinhead in the perioral region and also on the neck

Histologic examination on May 3, 1947, showed pronounced hyperkeratosis and an increased granular layer in some areas Classic corps ronds and grains were present in some sections There were lacunas just above the basal cell layer and also within the prickle cell layer in many areas The histologic diagnosis was keratosis follicularis (Darier's disease)

At the clinic the patient received injections of liver extract, potassium arsenite solution (Fowler's solution) and vitamin A by mouth During the summer of 1947 she also had ten intramuscular injections of a preparation containing 100,000 units of vitamin A, given triweekly, with little benefit Since Sept 4, 1947, she has been treated at my office Treatment has consisted of administration of a compound containing 200,000 units of vitamin A daily by mouth in combination with ox bile extract (bile salts) Six roentgen ray treatments were given to the supraclavicular regions and neck There has been moderate improvement However, the patient states that the condition is at its worst in the summer

thyroid therapy For four months there was no change in the nails By June 1946 there was definite improvement, which has been continuous At present all the nails have practically returned to normal

DISCUSSION

DR PAUL GROSS There is a definite relationship between the thyroid and the vitamin A metabolism In cases of hypothyroidism there is frequently a vitamin A deficiency The excellent therapeutic result obtained by Dr Fisher is noteworthy

DR EMANUEL MUSKATBLIT It seems to me that onycholysis is not always of the same origin Some of these cases have an occupational background In others a separation of the nail from its bed results when the patients constantly soak their hands in water In such cases removal of the cause results in a cure

DR HENRY SILVER I consider the point raised by Dr Muskatblit pertinent The role of continuous use of soap and water should not be underestimated, particularly in patients with systemic disturbances The condition in this case, with the manifest thyroid disturbance, may well fall in this group (Silver, H, and Chiego, B Brittleness of Nails, *J Invest Dermat* **3** 5, 1940)

DR ALEXANDER A FISHER In spite of this boy's washing his hands many times a day, he is improving with vitamin A and thyroid therapy Moreover, it is strong alkali which causes onycholysis, and he denies the use of strong soaps

Circumscribed Scleroderma (Treated with Promin®). Presented by DR HARRY B FEILER.

L S, a woman aged 74, has been complaining of pain, burning sensation and tightness of the skin of the chest In May 1946, she noticed a patch about 3 by 1½ inches (8 by 4 cm) in diameter, located on the right side of the chest, which was hard, white and glistening and was surrounded by a violaceous border At present the lesion is still of the same size The blanched area is somewhat softer and has the remnant of the violaceous border Recently a few linear lesions appeared above the involved area

The patient has been given polyvitamins by mouth, and, with this regimen, there was a disappearance of the leathery consistency in the lesion, but otherwise there was no change She has received intramuscular injections of 50,000 units of vitamin A every second day for three weeks without any noticeable improvement

For the past week promin® (sodium p,p'-diaminodiphenylsulfone-N,N'-didextrose sulfonate) jelly has been applied There developed dermatitis at the site of the lesion accompanied with pain and burning sensation Treatment with promin® was discontinued

DISCUSSION

DR DAVID BLOOM Morphea may disappear without treatment Unless the effect is rapid, one cannot prove that promin® is therapeutically useful in morphea

DR ALEXANDER FISHER If no improvement takes place with promin® I would suggest bismuth subsalicylate Dr John A Stokes first mentioned this type of therapy Several patients at the Skin and Cancer Clinic have improved with treatment with bismuth preparations

DR. CHARLES R REIN Dr Carol Wright and Dr Elmer Gross have had excellent results in the treatment of scleroderma with a bismuth preparation (bistrimate®) given orally

DISCUSSION

DR NATHAN SOBEL A diagnosis of familial benign chronic pemphigus (Hailey and Hailey) was considered in this case, but the diagnosis of keratosis follicularis was established on the basis of histologic findings The patient is presented because of the failure of the condition to respond to large doses of vitamin A and liver

DR SAMUEL M PECK There are two curious facts that stand out in the treatment of keratosis follicularis with large doses of vitamin A (1) there is a peculiar relation between keratosis follicularis and exposure to light, and (2) some patients who do not respond to oral therapy respond to injections

Exposure to sunlight causes aggravation of the eruption and, at times, vesiculation My patients learn soon enough not to go to the beach It is my experience that lesions on the exposed parts, such as the forehead, face and neck, are more resistant and clear much later than those in comparatively protected areas, such as the axillas It is evident that the light factor plays an important role

Some cases which do not respond to vitamin A therapy alone do respond to treatment with a combination of vitamin A and members of the vitamin B complex This fact was called to my attention by Dr Gross Vitamin B metabolism apparently plays a role in the second factor If some patients do not respond to treatment with vitamin A, it should be supplemented by injections of liver and large doses of nicotinic acid

DR CHARLES R REIN In other cutaneous conditions associated with vitamin A deficiency, the administration of large doses of vitamin A orally did not produce a beneficial effect until absorption from the gastrointestinal tract was implemented by the concomitant ingestion of dilute hydrochloric acid Such a regimen might be effective in treatment of this patient

DR HANS STORCH, Zurich, Switzerland (by invitation) A case of keratosis follicularis recently under observation at the University Clinic in Zurich has responded remarkably well to treatment with grenz rays

DR NATHAN SOBEL With respect to Dr Peck's remarks regarding exposure to light and keratosis follicularis, I can state that this patient's condition had been aggravated during the summer Since it is believed that sunlight has a bad effect on this condition, another patient under my observation was kept out of the sun's rays but failed to improve I also exposed a small area of the back of that patient to ultraviolet rays in erythema doses, but no new papules have formed I believe there must be some factor other than sunlight to aggravate the condition during the summer months The patient I presented tonight also failed to improve by avoidance of sunlight She has already been given injections of crude liver extract I shall, however, follow the suggestions of Drs Peck and Rein and try treatment with nicotinic acid and hydrochloric acid I may also try the use of grenz rays, as suggested by Dr Storch

Livedo Reticularis, with Recurrent Superficial Ulcerations of the Feet Presented by DR SAMUEL M PECK and DR KAI K LI (by invitation)

Purpura Annularis Telangiectodes (?). Presented by DRS PAUL GROSS and ELLEN REINER

Wilbert Sachs, M D, *President*
Henry Silver, M D, *Secretary*
April 17, 1947

Superficial Epitheliomas, Treated with Podophyllin Presented by DR JOHN GARB

M B, a man aged 73, was first seen on July 17, 1946, presenting three cutaneous lesions He had pneumonia in 1916 He has otherwise been in good health

The largest of the three lesions is located on the left lower border of the anterior part of the chest and epigastrium It is roughly round, 3 inches in diameter (7 5 cm) and dry, with a slightly raised border In that circle are several raised, crusted, irregular, dark red to purplish lesions, which are rough to the touch Most of the lesions have cleared with topical remedies and with exposures to ultraviolet rays, leaving a slightly darker but normal-appearing skin This lesion has been present for the past four years On the inner third of the right clavicle there is a similar patch 1 cm in diameter and an oval patch with axes of 7 and 5 cm on the left side of the back There is a scar in the midportion of the back as a result of an operation performed in 1945 for a carbuncle

The routine laboratory tests showed no abnormalities

Sections were taken from specimens of lesions on the front and back of the chest and examined histologically by Dr Charles F Sims The former showed a somewhat irregular epidermis At one point, extending down into the corium on the under surface of the basal margin, was a small mass composed of basal cells The vessels of the upper part of the corium were moderately dilated and surrounded by mild interstitial edema and a nonspecific cellular reaction From the histologic examination the diagnosis was superficial basal cell epithelioma

Microscopic examination of the specimen taken from the lesion of the back showed features of superficial dermatitis

An ointment containing 5 per cent podophyllin prepared with 8 Gm of castor oil and aquaphor® (an oxycholesterol-petrolatum ointment base), enough to make 2 ounces (57 Gm), was applied on January 30 to the lesions of the chest On February 1, the lesions became ulcerated and a soothing ointment was applied On February 18, the rim of the lesion on the frontal part of the chest was still visible but not raised On February 25, the upper part of the patch on the back was still elevated On March 4, an ointment containing 10 per cent, and on March 11 and 13, 20 per cent of podophyllin was applied to a few spots on the frontal part of the chest On March 31, the 10 per cent ointment was applied to a few spots on both lesions On April 10, the lesion on the back appeared healed except for slight roughness The lesion on the front part of the chest was flattened to the level of the surrounding skin surface The border was still visible because of the brownish pigmentation A section was taken from the pigmented border close to the scar of the original section which showed basal cell epithelioma The histologic examination by Dr A M Sala showed atrophy of the epidermis and moderate round cell infiltration of the corium which appeared somewhat edematous There was no histologic evidence of neoplastic tissue

DISCUSSION

DR MARION B SULZBERGER The lesions give the impression of a superficial epithelioma either entirely healed or in the process of healing Whether a recurrence will take place one cannot foretell Several points need be considered

A Case for Diagnosis (Epidermodysplasia Verruciformis?) Presented by DRS MAX JESSNER and CHARLES R REIN

E W, a man aged 21, presents an eruption of five years' duration It began as a few discrete lesions on the forehead and reached the present stage within a few months The patient has received various types of therapy, including peeling, administration of wart vaccine and roentgen irradiation, with no appreciable change

His parents are nonrelated He states that his older sister has wartlike lesions on the fingers which have persisted for the past several years

The eruption is most conspicuous on the face and consists of discrete, light brown, nonscaly papules varying in size from that of a pinhead to that of a pea Many of these lesions are made up of groups of smaller lesions, some of them taking on an annular configuration The lesions over the bearded portion of the chin are quite characteristic of verruca plana There is a solitary verrucous lesion, the size of a large pea, on the dorsum of the left hand Several of the lesions were destroyed by electrodesiccation and curettage, which resulted in keloidal scarring A lesion of the forehead was removed for microscopic examination Dr C F Sims reported that the epidermis was moderately verrucous There was some elongation and broadening of the rete pegs at many points Considerable vacuolation of the cells of the granular layer and the upper rete cells was observed No noteworthy changes were present in the corium

DISCUSSION

DR EMANUEL MUSKATBLIT The lesions impress me as ordinary verrucae planae What clinical features justify the other diagnosis?

DR HENRY SILVER I hesitate to make a diagnosis of epidermodysplasia verruciformis in this case, but I should definitely rule out verruca plana I admit that the histologic evidence, such as ballooning of the cells and the basket weave appearance of the epidermis, is characteristic These features, however, are not limited to epidermodysplasia verruciformis but are seen in other diseases, such as verruca senilis, mal de Meleda and molluscum contagiosum, and even in common warts We cannot, therefore, rely solely on the histologic evidence Because of our lack of knowledge regarding etiology of the disease, it is difficult and often confusing to separate the clinical varieties encountered These variants of localized or region-specific keratoses are often considered as separate entities on flimsy evidence It is highly probable that epidermodysplasia verruciformis of Lewandowsky and Lutz, Hoffman's verrucosis generalisata and possibly Hopf's acrokeratosis verruciformis are clinical variants of the same disease

The well developed cases of epidermodysplasia verruciformis are readily diagnosed Most of the characteristic features, such as the disseminated, verruca-plana-like lesions, the tendency to malignant transformation, the verruca-vulgaris-like lesions and the verrucous plaque formations, are usually present The case I presented before the Section of Dermatology of the New York Academy of Medicine was a fairly characteristic example of the disease (Epidermodysplasia Verruciformis, ARCH DERMAT & SYPH **45** 836 [Nov] 1941) Dr Rein's case lacks some of the clinical features I would therefore consider his case a forme fruste of the disease

DR PAUL GROSS In spite of the fact that the diagnosis epidermodysplasia verruciformis is still in doubt, I should definitely rule out the suggested diagnosis of verruca plana on clinical grounds

Certain superficial epitheliomas respond quickly to many forms of therapy Mild caustics and other superficial destructive measures may cure most superficial and small basal cell epitheliomas In evaluating any new therapy, one should keep in mind the ease with which nonspecific measures can remove these so-called carcinomas

Podophyllin is a peculiar substance which has some influence on mitosis As Maurice Sullivan, Lester S King and others have pointed out (in Wise, F, and Sulzberger, M B Yearbook of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc, 1946, p 510), podophyllin, like colchicine, somehow affects the nuclear metabolism and one sees many cases of arrested mitosis, all in the same phase—the metaphase, I believe It is, therefore, possible that podophyllin or podophyllotoxin may have some specific effect on the multiplying cells of the carcinoma and that the results achieved may be more than a mere nonspecific destructive action The action of podophyllin is well worth studying in relation to epithelial growth and deserves a good deal of further careful experimentation

DR FRANK E CROSS New methods of therapy that are simple and promising should be encouraged, on condition that they are as good as or better than the older ones Dr Sulzberger just stated that podophyllin seems to have a basic action in that it interferes with mitosis On the other hand, I take exception to his statement of the "simplicity of ordinary epitheliomas" It is true that a treatment of some basal cell epitheliomas is simple, in others, however, radical measures must be resorted to

DR WILBERT SACHS A biopsy specimen taken from the "healed" area will determine whether any carcinomatous tissue still remains

DR JOHN GARB The patient had the lesion on the left lower border of the chest and the epigastrium for forty years A biopsy specimen taken from the pigmented margin adjacent to the original histologic section did not show any epitheliomatous change The patient was not presented tonight as cured He will be kept under observation

Dermatitis Due to Gold, Successfully Treated with BAL (2,3-Dimercaptopropanol) on Two Occasions Presented by DR MARION B SULZBERGER

DISCUSSION

DR ADOLPH ROSTENBERG I used BAL in a case of a widespread dermatitis of unknown cause, and the result was excellent It required several weeks of treatment, but after one injection there developed a severe nitritoid reaction, such as is observed after administration of arsphenamine preparations I have never observed it since and wonder whether this reaction occurs commonly

DR DAVID BLOOM Before administration of BAL the cardiovascular status of the patient should be determined A few weeks ago I observed a patient who received BAL for suspected intoxication due to bismuth This patient, who received an excessive dose of BAL, had a severe reaction manifested by a sensation of burning and constriction about the mouth, face and chest The patient appeared rather ill It was later discovered that this patient had myocardial damage

DR MARION B SULZBERGER This patient was presented to demonstrate therapeutically the effectiveness of BAL in dermatitis due to gold One interesting feature in this case is that the BAL therapy has been effective twice The eruption got worse when BAL therapy was discontinued and then rapidly improved with readministration The therapy was stopped for the reasons given by Dr

DR DAVID BLOOM From the appearance of the lesions, it is difficult for one to make a diagnosis of epidermodysplasia verruciformis, but one has to favor this diagnosis because of the plaque formation on the face The vacuolation of the epidermal cells seems on histologic examination to support the diagnosis as presented, although such changes are reported also in verruca plana and in other keratotic and dyskeratotic conditions I should like to call attention to the type described in the French literature as *erythrokératodermie verruqueuse en nappes*

DR. CHARLES LERNER In my opinion this is a case of verruca plana, if I may judge from the lesions that I observed on the dorsum of the left hand

DR MAX JESSNER I have little to add to Dr Silver's remarks Dr Rein and I expected a difference of opinion about this case, and for this reason we presented the patient The question of whether epidermodysplasia verruciformis is a dermatosis *sui generis* has become acute again since W Lutz's article appeared in *Dermatologica* in 1946 Epidermodysplasia verruciformis had already once to fight for its existence and nevoid nature when it was confronted with verruca disseminata and verrucosis generalisata, respectively At that time it had, we believed, won the fight Such cases as Lewandowsky and Lutz's first one, which I saw, are impressive, and their nevoid and rather often precancerous nature ought not to be doubted A case not as widespread, with several epitheliomas, shown to me by Dr de Cholnoky, will be presented at a subsequent meeting It is the more or less abortive forms resembling clinically verruca plana which are difficult to diagnose, especially if the vacuolation of the rete cells is not outstanding and because of the fact that a certain degree of vacuolation may also be found in warts In the case presented it is the clinical aspect, especially the confluence of the lesions in some parts of the affected region, and the course of the disease, together with the histologic features, that favor a diagnosis of epidermodysplasia verruciformis

DR CHARLES R REIN I have learned that the patient's sister also had verrucous lesions on the hands If this point is confirmed, it will corroborate the diagnosis as presented The differential histologic diagnosis lies between verruca plana and epidermodysplasia verruciformis The clinical findings, history and course of the condition must be taken into consideration before a definite diagnosis can be established

Parapsoriasis Varioliformis Presented by DR FRANCES PASCHER

Juxta-Articular Nodes in a Patient with Neurosyphilis Presented by DR JULIUS H POLLOCK

Basal Cell Epithelioma of the Nipple of a Man Presented by DR NATHAN SOBEL

L S, a man aged 46, has been a patient at the Skin and Cancer Unit of the New York Post-Graduate Hospital since Sept 19, 1947 The duration of the lesion is not definitely known, but the condition has been present for at least several years When the patient was first seen at the hospital there was in the area of the right nipple a scaly and somewhat crusted noninflammatory lesion the size of a dime The diagnosis of carcinoma simplex (Paget's disease) of the nipple was considered At present the entire right nipple and adjoining areola show an infiltrated plaque with an irregular surface

The Wassermann reaction of the blood was negative on Sept 19, 1947 Microscopic examination made by Dr C F Sims, showed that the epidermis was eroded

Bloom There was slight albuminuria and a systolic blood pressure of 180 mm For that reason Dr Jessner thought it wise to discontinue the BAL therapy when the patient had improved

BAL is a powerful drug and one must be careful, particularly in patients with hypertension One good feature is that BAL is rapidly excreted, and the side effects are usually evanescent It is usual for the blood pressure to rise, however, this is variable, and I have often seen the blood pressure fall after BAL injections Because of the effect of BAL on blood pressure Dr Harry Gold of Cornell University expressed the belief that BAL might be valuable in treatment of certain peripheral vascular diseases It is effective also in allergic dermatitis and other conditions produced by certain metals and is often life saving in cases of allergic dermatitis due to mercury and arsenicals I would estimate that only about half of my patients with arsenical dermatitis have shown rapid and unequivocal improvement Theoretically one should expect a favorable response from BAL applied locally However, BAL is a strong cutaneous allergen, hence as a rule one cannot use it as an external application

A Case for Diagnosis (Sarcoid?) Presented by DR MAX BERKOVSKY

A Puerto Rican, aged 60, was admitted to the dermatologic service of the Metropolitan Hospital on March 20, 1947 There appeared on the left thigh a flat, sharply defined lesion the size of a dime, associated with some itching but no pain Similar spots appeared on all four extremities during the next three months The family history revealed that forty years ago the patient was intimately exposed to active tuberculosis in a relative who subsequently died of the disease The patient stated that to his knowledge he never had gonorrhea or syphilis

In 1932 he had an abscess of the left thigh which was opened and drained In 1939 cardiac decompensation developed Digitalis therapy was instituted, and the patient was discharged much improved In the fall of 1946 he was treated at the Harlem Hospital for a cough, and in three months he was discharged as cured He has lost 15 pounds (7 Kg) in the last ten years The only drug that he takes is feen-a-mint® (a laxative containing phenolphthalein) about twice a month

Physical examination reveals a well developed but poorly nourished man The systolic blood pressure is 180 and the diastolic pressure 90 The skin shows many nummular dark brown sharply demarcated flat-topped nodules with some infiltration They are symmetric and not tender and at present involve all four extremities and to some extent the chest and back

The Wassermann, Kahn and Kline reactions of the blood were negative Urinalysis showed no abnormalities Examination of the blood showed 82 per cent hemoglobin, 3,750,000 red blood cells and 12,200 white blood cells, with 40 per cent polymorphonuclear cells, 32 per cent lymphocytes, 15 per cent eosinophils, 11 per cent monocytes and 2 per cent basophils

Roentgenograms of the chest revealed a round shadow the size of a baseball in the region of the left hilus and extending into the anterior mediastinum This was diagnosed as a dermoid cyst, a teratoma or a benign cystic mass Roentgenograms of the hands showed no abnormalities The reaction to the tuberculin test was negative Histologic examination of specimens taken from the left thigh and left arm showed edema and hyalinosis of the papillae with perivascular infiltration of small round cells There was no evidence of tuberculosis The diagnosis from histologic study was chronic dermatitis of unknown cause

in one area Below it there was a large mass made up of groups and strands of basal cells The palisade layer was intact There was a slight inflammatory infiltrate in the midcutis

DISCUSSION

DR CHARLES F SIMS I have examined the slide, and there is no question that it is of basal cell carcinoma

DR HENRY SILVER I suggest that the condition be subjected to the Mohs method of therapy

DR FRANK E CROSS Cancer of the breast in the male is more malignant than is that in the female It is rather uncommon in the male and is usually of the prickle cell type I do not question the histologic report, but in view of the previous statement I feel that one must be more radical in therapy I should, therefore, suggest a wide excision of the nipple, followed by the making of serial sections of the specimen removed for further histologic study

DR CHARLES F SIMS Dr Cross's suggestion of a possible prickle cell epithelioma was not substantiated by the histologic findings

DR NATHAN SOBEL When first seen the lesion was scaly and crusted, and the diagnoses that were considered were chronic eczema, possibly Paget's disease and keratosis of the nipple Tonight the lesion looks clean and somewhat nodular, and it is difficult to make the diagnosis on clinical grounds alone

As Dr Cross stated, basal cell epithelioma of the nipple in the male is a rare condition Dr Arthur Hyman reviewed the literature and could find only the following references to its occurrence Elliott and Welland (ARCH DERMAT & SYPH **53** 322, 1946) reported not a single case of basal cell epithelioma of the nipple among 1,928 cancers of the skin In 1924, Wainright (*Arch Surg* **14** 844, 1927) reviewed 264 cancers of the male breast and found only 1 case of basal cell epithelioma in the series In this series there were only 6 prickle cell epitheliomas, so even prickle cell epithelioma of the nipple is rare Geschickter (Diseases of the Breast, Philadelphia, J B Lippincott Company, 1943, p 603) refers to a reported case of basal cell epithelioma in the female breast mentioned by Ewing Dr Hyman informed me that he has personally seen 1 case of basal cell epithelioma of the male nipple and adjoining areola which was clinically diagnosed as Bowen's disease

After the lesion is removed, serial histologic sections will be studied

FOLLOW-UP NOTE Serial sections showed only basal cell epithelioma

Multiple Pigmented Nevi Presented by DR CHARLES WOLF

Poikiloderma of Civatte Presented by DR HARRY B FEILER

PHILADELPHIA DERMATOLOGICAL SOCIETY

J M Schildkraut, M D, *Chairman*

Douglass A Decker, M D, *Secretary*

April 18, 1947

Herpetic Stomatitis and Vaginitis (Pemphigus?) Presented by DR JOHN F WILSON

Scleroderma with Calcinosis Presented by DR CARMEN C THOMAS and (by invitation) DR DAVID KREMER

DR FREDERICK R SCHMIDT At one time my co-workers and I collected 9 cases of alopecia areata which recurred regularly in September and March of succeeding years, which was apparently a type of arterial spasm, due to poor nutrition of the end arteries

DR E M SMITH JR It would be impossible for the patient to pull out the hair I have seen two recurrences, and they are absolutely the same, in that they run right down the middle of the scalp and extend only to the right side and not the left

Multiple Nevi (Adenoma Sebaceum) (Dermatosis Papulosa Nigra and Fibroma Pendulum) in a Negro Presented by DR E A OLIVER and (by invitation) DR E LORANT and DR A B HENNINGSEN

Lymphoblastoma Cutis with Poikilodermatous Changes Presented by DR F E SENEAR and STAFF

Ainhum of Two Years' Duration in a Negro Aged 66 Years Presented (by invitation) by DR MAURICE OPPENHEIM and DR DAVID COHEN

A Case for Diagnosis (Unilateral Vascular Nevus? Angioma Serpiginosum? Schamberg's Disease?) Presented by DR F E SENEAR and STAFF

Ichthyosiform Erythroderma? Presented by DR S ROTHMAN and (by invitation) DR J H MCCREARY

Localized Myxedema, Pretibial, Following Thyroidectomy Presented by DR F E SENEAR and STAFF

Probable Triple Symptom Complex of Behcet, Scrotal Tongue Presented by DR F E SENEAR and STAFF

A I, a white housewife aged 25, was shown at the December meeting of this society with a condition for diagnosis She gave a five months' history of recurrent ulcerative lesions of the mouth which had not responded to various local treatments or to intravenous treatment for a diagnosis of "trench mouth" made prior to admission At the time of presentation, she showed a marginal scrotal tongue with whitish patches of membrane extending from some of the crypts of the tongue, as well as scattered on the buccal mucous membranes These were relatively easily removed, leaving superficial tender ulcerations without bleeding and surrounded by an erythematous halo Direct examinations did not reveal mycelia During the discussion the following diagnoses were mentioned as possibilities (1) aphthous stomatitis, (2) moniliasis, (3) eruption due to drugs, (4) Behcet's triple symptom complex and (5) scrotal tongue

Medical consultation revealed nothing contributory The urine was normal, blood cell counts were normal, the results of the serologic test for syphilis and examination of the chest were all negative Examination by the gynecologic consultant showed only chronic cervicitis Repeated cultures from the mouth lesions failed to demonstrate Monilia, although cultures from vaginal discharge on one occassion did grow mucoid colonies with budding forms on microscopic examination On one occasion, the patient complained of soreness about the vulva,

and examination in our department revealed superficial ulcerations about the labia minora and majora

On about the first of February, the patient was found to have decided injection of the right conjunctiva diagnosed as episcleritis by the ophthalmologic consultant This was considered consistent with, though not diagnostic of, Behcet's syndrome of the eye She stated that she had had one previous similar, though less severe, attack of ocular inflammation about five weeks ago

Perniones and Livedo Reticularis in a Poliomyelitic Limb Presented by DR F E SENEAR and STAFF

DISCUSSION

DR M R CARO The sections were not typical of tuberculosis or tuberculid, though there were round cells which extended deeply into the fat

DR STEPHEN ROTHMAN I was very much impressed with this case because I saw quite a few after World War I in patients who had nerve injuries It shows what a profound effect trophic ulcers have on vasomotor action

DR J F MADDEN, St Paul In our experience with poliomyelitis, my co-workers and I have noted that the patients have more cutaneous changes than the normal person During the acute stages in which the Sister Kenny method of therapy is used the patient often shows miliaria from the hot applications

DR F E SENEAR When I first saw this patient a couple of weeks ago, I thought that he had an exaggerated example of erythrocyanosis frigida crurum that the English have written about This is the first time I have seen one with so much inflammatory element that it simulated erythema exfoliativa Dr Brunner called our attention to the fact that Telford had pointed out that just this type of reaction does occur, particularly in the wasted limbs of persons who have had poliomyelitis I think, as Dr Rothman indicated, that it is a nerve injury that predisposes to this type of reaction, which is less intense than erythema exfoliativa

Eosinophilic Granuloma? Presented by DR S ROTHMAN and (by invitation) DR J H MCCREARY

Since the age of 2 years, the patient, an 11 year old white girl, has been almost continuously sick with swelling of lymph nodes and with ulceration of the overlying skin on the head, neck and thorax The appearance of each new lesion has been accompanied with a temperature of 99 to 104 F, pain, tenderness, erythema and some swelling over the affected gland The overlying skin became red and shiny until spontaneous rupture occurred A seropurulent exudate appeared, and a crust was formed over a deep crater After rupture of the "abscess," the systemic symptoms disappeared and the temperature returned to normal There is a tendency toward slow healing with granulation and scar formation Since an operation two years ago for the removal of a group of cervical glands, the motion of the shoulders and neck has been restricted because of pain

Just previous to the onset of the present illness, the patient had measles and mumps at the same time During this illness the adenitis of the right submaxillary glands developed This adenitis failed to resolve, and formed an ulcer which persisted over twenty months Abscesses of nearby nodes followed in a similar characteristic course

Roentgen therapy seemed to accelerate healing, with remissions of the symptoms for as long as a year Dosages of the many courses of roentgen rays she received

Blastomycosis with Pulmonary Involvement. Presented by DR CARMEN C THOMAS and (by invitation) DR G H WELLS

Cutaneous Diphtheria Presented by DR CLARENCE S. LIVINGOOD and (by invitation) DR HARVEY BLANK

C L, a white man aged 25 years, presents healed, round scars on both legs, approximately 1 inch (2 cm) in diameter, with brownish, pigmented, atrophic centers On July 10, 1944, five weeks after the patient's arrival in Burma, ulcers appeared on both legs On August 3 he was admitted to the 69th General Hospital, Assam, India, with multiple, punched-out ulcers with a tough black eschar and a rolled bluish red border On October 1 numbness and weakness of the fingers, toes, hands and feet appeared By October 31 the skin had healed, and by December 30 the neuritic symptoms had cleared

The smears taken from the ulcers did not show fusiform bacilli or spirochetes Cultures were not available, but virulent Corynebacterium diphtheriae were cultured from many other patients with the same type of lesion

The patient was treated with various bland local measures and bed rest As the result of his Schick test was negative, no antitoxin was given

DISCUSSION

DR CLARENCE S LIVINGOOD This is a patient whom Dr Blank saw from the onset of his illness The scars are typical postdiphtheritic ones Other ulcerative lesions can leave scars, but with experience one can identify the postdiphtheritic type We had difficulty in convincing our colleagues that cutaneous diphtheria produced ulcers that are diagnostic Any dermatologist who is accustomed to seeing and making fine distinctions between ulcerative lesions can make this diagnosis without difficulty Anthrax, first degree burns and trophic ulcers can produce somewhat similar scars, but I do not believe that any other conditions produce ulcers of this type

A Case for Diagnosis (Poikiloderma Atrophicans Vasculare?). Presented by CAPTAIN ROBERT L GILMAN, United States Navy

Parapsoriasis en Plaques Presented by DR LEWIS M JOHNSON

R J, a white man aged 19 years, noticed an eruption on his lower extremities shortly after an attack of severe bronchitis in the spring of 1945 There have been no subjective symptoms The lesions started as small macules and gradually progressed in size and number and occurred on his upper extremities together with an associated loss of pigment During the summer of 1946 the eruption on his upper extremities faded considerably, but recurred during the past winter The history reveals no prolonged ingestion of drugs prior to the onset of the eruption except for "drops" for his heart The patient is well built and presents variously sized, round and oval, pinkish to copper-colored, macular lesions, some of which have a fine scale and a reticulated appearance They are more profuse on the lower extremities, those on the upper extremities have an associated patchy loss of pigment in the surrounding skin These lesions, when viewed with filtered ultraviolet rays ("black light"), are darkened and more pronounced on the lower extremities and have a faint fluorescence on the upper extremities The results of the rest of the physical examination were essentially normal except for a soft mitral systolic murmur, a chronic macerated and fissured eruption between the toes of both feet and hyperhidrosis of the hands and feet

DR J M SCHILDKRAUT Port wine stains are notorious for their failure to respond to roentgen rays But Dr Pfahler and I have recently had infants with such lesions that did respond and we are of the opinion that if radiation is used early these lesions may respond

Sarcoid Solitary Lesion on the Nose Presented by DR CARROLL S WRIGHT and DR E R GROSS

Acne and Comedos in an Infant 8 Weeks of Age Presented by DR. H H PERLMAN

Tuberculosis Verrucosa Cutis on the Neck. Presented by DR MEYER L NIEDELMAN

Reuben Friedman, M D, *Chairman*

Douglass A Decker, M D, *Secretary*

Nov 21, 1947

A Case for Diagnosis (Cutaneous Diphtheria?) Presented by DR LEWIS M JOHNSON (Lancaster, Pa)

A M B, a white woman aged 28, presents a healing ulcer in the right lower quadrant of the abdomen, early necrotizing lesions on the inner side of the left thigh of three days' duration and numerous depressed scars on the left wrist, on the left breast, in the left groin, on the left leg and on the left side of the abdomen She also has a tumor on the left lower part of the back

The present condition developed on Oct 12, 1946, with a "red spot" on the left wrist which formed a blister, turned black, ulcerated and healed, leaving a deep scar Since then other similar lesions have developed When the ulcers develop, she sometimes has painful joints, malaise, nausea and severe menstrual cramps

The serologic tests for syphilis were negative A complete blood count revealed 76 per cent hemoglobin, 3,620,000 erythrocytes, 7,200 leukocytes, 75 per cent polymorphonuclear leukocytes, 23 per cent lymphocytes, 1 per cent monocytes and 1 per cent eosinophils

The microscopic examination of the biopsy section revealed a focus of incomplete necrosis involving essentially the stratified squamous epithelium and its immediate underlying connective tissue This reaction was associated with an inflammatory cell infiltration consisting essentially of eosinophils, plasma cells, lymphocytes and a few polymorphonuclears (neutrophils) This infiltrate occurred chiefly about the blood vessels in the subepithelial areas In some areas the walls of the blood vessels showed a similar infiltration There was also a granulomatous reaction resembling a foreign body reaction Numerous foreign body giant cells appeared in these lesions, and in many instances they contained greenish crystals New blood vessel formation was a prominent feature and appeared to be demarcating the area of necrosis The diagnosis was necrosis of the skin

DISCUSSION

DR CLARENCE S LIVINGOOD This could be cutaneous diphtheria. It might be a factitial eruption caused by an escharotic chemical, such as phenol or saponated cresol solution, but from a clinical standpoint the most likely diagnosis

A complete blood cell count revealed 93 per cent hemoglobin (14 73 Gm), 4,870,000 erythrocytes, 11,600 leukocytes, 71 per cent polymorphonuclear leukocytes and 29 per cent lymphocytes The result of the Kline test of the blood for syphilis was negative The potassium hydroxide preparation of the scales did not reveal fungi A urinalysis showed no abnormalities

DISCUSSION

DR MEYER L NIEDELMAN I suggest the diagnosis of erythema multiforme perstans The lesions have been present for two years, are sharply marginated and on diascopic pressure become rather light, and the surrounding tissue seems to have some pitting edema

DR FRITZ CALLOMON (by invitation) The diagnosis of parapsoriasis appears acceptable This form corresponds to Brocq's erythrodermie pityriasique en plaques disseminees and the yellowish color with the English description of Radcliffe Crocker's xanthoerythroderma perstans Although the lesions of Brocq's disease usually persist unchanged over many years, seasonal changes were observed by Civatte, White and Brocq himself, who described obvious remission during the summer and exacerbation during the winter months (Jadassohn, J Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol 7, pt 1, p 388)

DR BERTRAM SHAFFER This eruption has a peculiar artificial appearance I suggest the diagnosis of factitial eruption The lesions are sharply demarcated and regular, and all of them are disposed on parts of the body accessible to the patient

DR DONALD M PILLSBURY I agree with Dr Shaffer The pharyngeal and corneal reflexes are absent Some of the lesions have disappeared, which is against the diagnosis of parapsoriasis If it turns out that the patient has parapsoriasis, I suggest a trial of anthralin to the point where it produces some reaction This case is similar to one Dr Kulchar had in our clinic some years ago, the only one of parapsoriasis which cleared up with treatment with anthralin (dihydroxyanthranol)

DR LEWIS M JOHNSON, Lancaster, Pa I cannot agree that the patient produced the lesions on the backs of the arms, nor can I understand the depigmentation I thought of a fixed type of eruption when I saw him first in November I shall let you know the report of the biopsy

NOTE—The diagnosis from the biopsy was parapsoriasis (Lancaster General Hospital)

Sporotrichosis Presented by DR J M SCHILDKRAUT, Trenton, Pa

Recurrent Lupus Erythematosus Presented by DR H E TWINING

J C, a Negro man aged 30 years and well nourished, presents sharply marginated, eczematous, slightly scaly patches of dermatitis on the cheeks, nose and mucous membranes of the mouth of about four months' duration The original lesions almost completely disappeared with treatment with bismuth subsalicylate injections and liver This is the third recurrence, all the lesions appearing at the original sites A small, erythematous area developed on the bridge of the nose in 1943 This was diagnosed as eczema Three months later it recurred with erythematous scaly lesions sharply demarcated on the nose and cheeks

A roentgenogram of the chest did not show tuberculosis Treatment with injections of bismuth compound and liver was successful in previous attacks but produced no improvement in the present one

is cutaneous diphtheria The patient has numbness and tingling of her hands and some weakness She had a severe sore throat about two months after the first lesion developed I suggest careful bacteriologic studies on the most recent lesion, done with the full realization that it is difficult to isolate the Klebs-Loeffler bacillus from the skin even when it is present A spinal fluid examination should be done, and if the patient has an elevated spinal fluid protein, it would lend weight to the thought that the numbness and tingling of the hands represent a neurologic complication of the cutaneous diphtheria

DR DONALD M PILLSBURY I saw this patient after Dr Livingood did, and our initial joint reaction was that culture for corynebacterium diphtheriae was indicated The usual sharp borders of a factitial eruption produced by an escharotic are also characteristic of many diphtheritic ulcers of the skin, and the differentiation may be difficult I suggest, in addition, very careful clinical study from the standpoint of peripheral neuritis or other late changes due to diphtheria toxin If any further collateral evidence of diphtheria is uncovered and if a factitial origin can be ruled out, I suggest administration of diphtheria antitoxin, even if the cultures are negative As has been pointed out, recovery of the organism may be difficult in the hands of even the most experienced bacteriologist, especially when the lesion is old or when local treatment, such as applications of penicillin, has been given

Sulzberger-Garbe Disease (?) (Exudative Discoid and Lichenoid Dermatosis) Presented by DR LOUIS GOLDSTEIN and (by invitation) DR J FERNANDEZ

H K, a white man aged 43, presents papulomacular eruptions on the trunk and extremities which are retiform in character The papules are large, flat topped and reddish-yellow or darker, with mild scaling The patient has had attacks of this condition since 1930 He was hospitalized in April 1947 for an intensely pruritic dermatosis of several months' duration He was discharged much improved after three weeks of treatment Several days after discharge the dermatosis recurred, and he was again hospitalized for five weeks and was discharged much improved Several days later the condition recurred again, and it has remained until the present time

A urinalysis showed occasional leukocytes, epithelial cells and some mucus Complete blood counts revealed 3,890,000 to 4,060,000 erythrocytes, 10,000 to 14,000 leukocytes, 60 to 82 per cent polymorphonuclear leukocytes, 16 to 33 per cent lymphocytes, 1 to 2 per cent monocytes, and 8 to 15 per cent eosinophils The blood sugar was 99 mg per hundred cubic centimeters of blood The urea nitrogen was 13 5 mg The serologic tests for syphilis elicited negative reactions On April 21, 1947, Dr Weidman reported the biopsy specimen to show psoriasis

The patient has been treated with coal tar solution N F, boric acid, amobarbital sodium (sodium amytal®), tripelennamine hydrochloride (pyribenzamine hydrochloride®), protein hydrolysate, starch baths and bismuth sodium triglycollamate (bistrimate®), with improvement

DISCUSSION

DR CHARLES R REIN, New York (by invitation) I agree with the diagnosis

DR MAX JESSNER, New York (by invitation) This condition was unknown in Europe but I have seen many cases in New York I suggest that the patient be treated with arsenic or be sent to Arizona, where most of these eruptions clear up

DISCUSSION

DR CHARLES R REIN, New York (by invitation) I have used bismuth sodium triglycollamate (bistrimate®) in a number of conditions, including lupus erythematosus, lichen planus, verruca and granuloma annulare Best results were obtained in patients with lupus erythematosus Two patients with this condition showed no improvement after many intramuscular injections of bismuth subsalicylate but responded well to oral treatment with bismuth sodium triglycollamate This preparation was also efficacious in some patients with acute generalized lichen planus, but the results in the other diseases were disappointing

DR H E TWINING I tried bismuth sodium triglycollamate in this patient but had to discontinue it because of the occurrence of stomatitis and gingivitis Has Dr Wright seen many patients who cannot tolerate this drug?

DR CARROLL S WRIGHT My co-workers and I have the same percentage of intolerance with this preparation as with bismuth given in any other form

DR MEYER L NIEDELMAN At the last Atlantic Dermatological Conference suramin sodium (naphuride®) was mentioned for the treatment of lupus erythematosus It would be worth while to try it in this patient, if bismuth preparations prove ineffective

DR STEPHEN WHELAN (by invitation) In a total of about 25 patients with discoid lupus erythematosus my co-workers and I have used bismuth sodium triglycollamate in the past year and a half and we have not had the favorable results that Dr Wright and Dr Gross have reported We had 2 cases of hypertrophic lichen planus with good results in which the disease had not responded to bismuth compound administered intramuscularly

Multiple Large Keloids. Presented by DR MEYER L NIEDELMAN

E R, a white man aged 25 years, has a large, thick, keloidal band on his neck It is lobulated and adherent and limits the motion of the chin There are a number of small keloids on the cheek, chest, back and arms and on the vaccination site There are no lesions on the lower extremities On the forehead, cheeks and nose there are numerous hyperpigmented macules from pinpoint size to pea size, which the patient stated have been present since birth He had a burn from hot water on the neck at the age of 8 years, the past history is otherwise normal At the age of 12 the patient first noticed the keloids about the neck Shortly thereafter papules developed on the right side of his face, which subsequently developed into keloids He sustained a human bite on the sternal area at the age of 16, which developed into a keloid

In 1943, at another institution, the entire keloid on the neck was surgically removed, sutured and treated with roentgen rays This region shortly grew larger than the original In 1944 the keloid on the left side of the neck was similarly treated, that on the right side of the neck was operated on in September 1944, with a skin graft from the right thigh A keloid developed at the donor site

DISCUSSION

DR. J P SCULLY (by invitation) This patient shows two different types of scar The question arises whether endocrine disturbances are a factor in the production of keloidal change and whether, if further surgical attempts were made in this case, it might be well to attempt the coincident injection of diethyl

DR STEPHEN T WHELAN What type of arsenic does Dr Jessner use?

DR MAX JESSNER, New York (by invitation) I inject a 1 per cent solution of arsenic trioxide with 2 per cent phenol, starting with 0 25 cc daily and increasing to 1 cc daily

DR CLARENCE S LIVINGOOD I have no better diagnosis to offer than Sulzberger-Garbe disease, but I always feel dissatisfied with that diagnosis This patient is similar to one of mine whose eruption cleared up, partly because of hospitalization and partly because of therapy of various types The most notable thing about his course was that there would be a flare-up following an infection of the upper respiratory tract or the injection of an autogenous vaccine in a very small dose

Mycosis Fungoides Presented by DRS CLARENCE S LIVINGOOD and (by invitation) J P SCULLY

W B, a white man aged 82, was first seen on Oct 7, 1947, with the chief complaint of "sore on the back" which had been present for four or five months The process was said to have begun as a "small pimple" between the scapulas which the patient attributed to an insect bite received at the seashore At the time of the first visit, the patient presented a firm, reddish, indurated lesion measuring 4 fingerbreadths in diameter, between the scapulas The center was slightly raised and purplish, but gave no evidence of breakdown of tissue or fluctuation During a subsequent period of two weeks' observation, some exudation and a suggestion of superficial breakdown of skin were evidenced Three weekly injections of 300,000 units of penicillin in oil and wax were without effect on the process

The general physical examination disclosed nothing significant except a palpable liver edge 2 fingerbreadths below the costal margin There was no splenomegaly and no generalized or localized adenopathy The patient complained only of slight itching

The results of urinalysis were normal The serologic tests for syphilis elicited negative reactions A complete blood count revealed 79 per cent hemoglobin, 3,950,000 erythrocytes, 7,750 leukocytes, 58 per cent neutrophils, 3 per cent eosinophils, 34 per cent lymphocytes and 5 per cent monocytes, the color index was 1 01

Biopsy was reported to indicate lymphoblastoma and probable mycosis fungoides (The punch biopsy wound healed promptly)

The patient was given 600 r of roentgen rays in doses of 100 r over a period of sixteen days Exudation ceased after the second treatment, the induration regressed and the lesions flattened within two weeks

DISCUSSION

DR FRED D WEIDMAN When I first looked at the lesion, I thought that it might be Bowen's disease that had been overtreated The sections show that there is a reticuloendothelial disease, but I cannot quite make myself think that it is mycosis fungoides The epidermal changes are not sufficiently hyperplastic I think that it would come closer to being Spiegler-Fendt sarcoid, even though clinically that diagnosis would not quite fit But there are many of these reticuloendothelial disturbances that cannot be forced into some particular niche or pigeonhole that dermatologists have made Just as in Hodgkin's disease, there are atypical cases, and I think that this is one of them I cannot go further than to say that it is an abnormality of the reticuloendothelial system perhaps closer to Spiegler-Fendt sarcoid than to anything else

stilbestrol or male sex hormone during the postoperative period It was suggested that one lesion, possibly the one on the sternum, be excised in trial treatment and then some type of therapy determined In one case irradiation was suggested I should like to see diethyl stilbestrol or some similar preparation tried in order to determine whether the keloidal aftermath might be prevented

DR IRA L SCHAMBERG Are keloids ever seen before puberty? Children suffer all sorts of trauma, and, if they are not seen, Dr Scully's suggestion has some merit

DR DONALD M PILLSBURY I have seen many keloids in children

DR MAX JESSNER, New York (by invitation) I had a keloid when I was a small boy, but not since then Keloid formation is due to a "fibrotic" tendency of the organism, and that may change I do not believe that we know the reason for this, but many things have been suggested There has been a report by a physician who cured keloids by the administration of sodium fluoride (Callam, M *Munchen med Wchnschr* **82** 1534, 1935) I tried it in a case and had the impression that it did good I was afraid, however, to give it in large doses

CAPTAIN ROBERT L GILMAN, United States Navy I have seen keloids in children 4 to 8 years of age

DR THOMAS BUTTERWORTH, Reading, Pa Keloids do occur in children I am treating a keloid now in a youngster The statement occurs in some books that keloids tend to undergo involution after the menopause I have seen a keloid develop in the breast of a school teacher about 55 years of age For the case presented today I recommend Dr H J Smith's 2 per cent menthol in cottonseed oil with massage

DR DOUGLASS A DECKER, Allentown, Pa Dr Smith stated that the menthol and cottonseed oil preparation helps only those patients with itching or pain in the keloid

J M Schildkraut, M D, *Chairman*

Douglass A Decker, M D, *Secretary*

May 16, 1947

Psoriasis, with Extensive Koebner Phenomenon Induced by Systemic Reaction to Sulfadiazine Applied Locally to Burn Presented by DR LESLIE NICHOLAS and (by invitation) CAPTAIN RAYMOND R SUSKIND

Trichophyton Purpureum and Monilia Infection of the Hands, Feet and Nails Moniliasis of the Tongue Presented by DR LESLIE NICHOLAS and (by invitation) CAPTAIN RAYMOND R SUSKIND

Pigmented Purpuric Lichenoid Dermatitis Presented by DR LOUIS GOLDSTEIN

S W, a white man aged 29 years, presents on both legs many smooth, small, slightly elevated papules, some of which fuse into poorly marginated patches They are reddish brown The condition began about six months ago on the lateroanterior aspect of the left leg as a reddish, flat, papular, quarter-sized lesion with no subjective symptoms and gradually progressed to the present size

DR. MAX JESSNER, New York (by invitation) It is impossible to make a histologic diagnosis in the early stage of mycosis fungoides, since there is nothing characteristic histologically at that time Dr John Garb is treating patients with mycosis fungoides with antimony potassium tartrate U S P, and the results have been astonishing The patients react promptly to the therapy

DR J P SCULLY (by invitation) The diagnosis was made by exclusion I could think of no other lymphoblastoma that would produce no other systemic manifestations without other evidence of disease and persist for six months

Extensive Pityriasis Lichenoides et Varioliformis Acuta (Mucha-Habermann) Presented by DR REUBEN FRIEDMAN and (by invitation) DR HERBERT KAPLAN and DR JOHN B ROXBY JR

DISCUSSION

DR DONALD M PILLSBURY This is an unusually extensive and good example of this disease Whenever I see a patient with this disease, I am amazed that it can be so confidently classified in the textbooks in the parapsoriasis group There are many features of it which suggest a subacute infection, or at least a local reaction to the products of some infection I should like to hear Dr Blank discuss whether or not any such cases have been studied from the standpoint of a virus origin, I do not recall any such reports

DR HARVEY BLANK (by invitation) As far as I know, this particular disease has not been investigated recently along those lines At the moment, one of the means of investigation of such a case is to put the vesicle material directly on the little screens to be used in the electron microscope, and it is now possible within a matter of hours to differentiate smallpox from chickenpox Dr Geoffrey W Rake, of the Squibb Institute, has worked this out in considerable detail and is interested in material from any questionable case

DR. REUBEN FRIEDMAN Fluid from several of the vesicles was inoculated into the scratched cornea of a rabbit, with a negative reaction

DR LOUIS GOLDSTEIN Did this patient have lesions in the oral cavity in the acute stage?

DR REUBEN FRIEDMAN No Three days ago papular hemorrhagic lesions developed on the roof of the mouth and pigmented petechial lesions on the palms and soles

Multiple Recurrences of Infectious Syphilis Over Nineteen Years, Granuloma Inguinale Presented by DR HERMAN BEERMAN and (by invitation) DR MORTIMER S FALK

P D, a white man aged 40, presents pinkish verrucous-appearing hypertrophic growth on the ventral surface of the coronal sulcus, negative for Treponema pallidum on dark field examination The patient had primary dark field-positive syphilis in February 1928 He was treated with arsenical and bismuth preparations Dark field examinations were made on several occasions—December 1930, November 1932, April 1934 and November 1938, all with positive results (This case was first reported by Pariser [*J A M A* **113** 1206 (Sept 23) 1939]) The original lesion, however, did not heal completely at any time Granuloma inguinale was suspected as early as 1934 and a few injections of antimony potassium tartrate were

DISCUSSION

DR FRED D WEIDMAN I think we were all struck by the extremely lurid color of these lesions, in six months there certainly ought to be some pigmentation, yet there is not In the sections there is not any sign of hemorrhage to explain the extreme redness nor is there any pigment One must explain the redness on some other basis than that, and it is known that sometimes infiltrations of cells will produce a red color, for example, the small red kidney in chronic interstitial nephritis There is not any particular vascular hyperplasia, and there is no hemorrhage, but there is something different in the constitution of the cells which in the aggregate makes them red That was one of the things that puzzled me in this case Microscopically certain features suggest lichen planus, like the sharp demarcation of the zone underneath, but cellular infiltration is sparse for that, considering that these are fresh lesions, yet they are so highly elevated and delicately nodular or papular They are not in a regressive stage They are not atrophic lesions If this were lichen planus it would have to be atrophic lichen planus, and that is contrary to what this patient presents There are many histiocytes, and I do not know what the significance of those may be except that they tend to assist in eliminating lichen planus as a diagnosis The grouping is not discoid, as it should be in Majocchi's disease, and the lesions are not hemorrhagic In this type there should be some pigmentation There is a slight scaliness, but in the Gougerot-Blum complex I think that there should be more scaliness than is shown here I think that this is a puzzling case, and I cannot give a specific diagnosis

A Case for Diagnosis (Leukemia?) Presented by DR THOMAS BUTTERWORTH, Reading, Pa

Extensive Verruca Plantaris, Verruca Vulgaris Presented by DR J M SCHILDKRAUT, Trenton, N J

DISCUSSION

DR C S LIVINGOOD I suggest that the patient soak his feet daily in a solution of formaldehyde It is well to use 4 per cent formaldehyde for only a minute or so at first and gradually increase the time to four or five minutes, depending on the reaction

DR THOMAS BUTTERWORTH, Reading, Pa I often advise patients to apply 60 per cent salicylic acid paste and bandage the foot for about three days and then rub in 30 per cent salicylic acid paste nightly with the round head of a clothes pin, this seems to be effective

DR ISADORE ZUGERMAN Has the patient had bismuth sodium triglycollamate?

DR J M SCHILDKRAUT, Trenton, N J He has had bismuth subsalicylate injections

DR THOMAS BUTTERWORTH When treating a patient with formaldehyde solution, one must be sure that the fluid is not much more than a ¼ inch (0 64 cm) deep

Tuberculosis Verrucosa Cutis Presented by DR SIMON KATZ and (by invitation) DR PETER HORVATH

Trichophytosis Barbae Presented by DR M H SAMITZ and (by invitation) DR LAWRENCE KATZENSTEIN

Résumé of Clinical Course

Date	Number of Injections	Drug	Serologic Reaction	Progress Note
2/29/28	. .	....	Kolmer 44 Kahn positive	Dark field-positive penile lesion
2/29/28-12/20/28	7	Arsphenamine Bismuth arsphenamine sulfonate	Kolmer negative	Patient lost from observation
9/19/30-9/25/30	2	Neoarsphenamine	Kolmer negative	Dark field-positive penile lesions
2/12/32 2/26/32	3	Bismuth subsalicylate	Kolmer negative	No clinical relapse
11/21/32	9	Trisodium arsphenamine sulfonate	Kolmer negative	Indurated, ulcerative penile lesion swarming with spirochetes, lesion was at same site as original monorecidive
1/19/33	9	Trisodium arsphenamine sulfonate, bismuth subsalicylate	Kolmer negative	
6/15/33 12/8/33	. 10	Trisodium arsphenamine sulfonate		Glans penis inflamed, ulcerative lesion
	10	Bismuth subsalicylate		
4/17/34 3/20/36	20	Trisodium arsphenamine sulfonate	Kolmer 00	Lesion on left side of glans penis, dark field-positive for T pallidum
	26	Bismuth subsalicylate	Kolmer 44 on 5 tests, 10/11/35 to 1/16/36	
8/13/34	3	Antimony potassium tartrate	Negative (cerebrospinal fluid) 1/24/36	On 6/19/34 inoculations (rabbit) were reported positive for T pallidum, lesion did not respond to therapy, possibility of granuloma inguinale considered
2/7/35	8	Fuadin®	Kolmer 44	Dark field-positive perianal condyloma and multiple indurated purulent secreting penile ulcers, condyloma healed under treatment
11/1/38	8	Arsphenamine	..... .	
8/1/39	3	Bismuth subsalicylate	Kolmer 44	
11/7/38	.	.. .		Ducrey test positive, Frei test negative
1/28/42 2/9/42	3	Bismuth subsalicylate	Kolmer positive	Patient returned with granulomatous lesion on frenulum which he stated had been present since original visit (14 years), dark field-negative for T pallidum, smear revealed presence of Donovan bodies
	3	Antimony potassium tartrate		
2/47	60	Penicillin, 2,400,000 units	Negative	Dark field-positive primary syphilis (diagnosed and treated in another institution)
10/2/47	.		Kolmer negative Kline negative	Patient returns with verrucous-appearing hypertrophic growth on ventral surface of coronal sulcus, dark field-negative for T pallidum
10/3/47	. . .			Biopsy granuloma inguinale

Pityriasis Rubra Pilaris Presented by DR CARROLL S WRIGHT and DR MEYER L NIEDELMAN

E F, a Negro woman aged 39 years, first had a severe sore throat and a painful right shoulder about two months ago She used a gargle several times daily, consisting of a solution of 1 teaspoonful of salt and several drops of iodine About two weeks ago swelling of the face, puffiness of the eyes and scaling of the scalp developed The eruption on the arms and body followed After the eruption appeared she received several injections of an unknown substance There is an acute inflammatory dermatitis of the face and edema of the periorbital areas with pronounced conjunctivitis The scalp and other hairy areas show scaliness On the extensor surfaces of the arms, shoulders, nucha and legs is a widespread discrete follicular keratotic eruption There is little itching There is no history of ingestion of drugs The Wassermann reaction of the blood for syphilis was negative

DISCUSSION

DR. HERMAN BEERMAN This is lichen planus

DR STEPHEN T WHELAN (by invitation) Some manifestations of the disease are incompatible with the diagnosis of lichen planus The process began on the face with edema and scaling, shortly after the patient had been to the hair dresser She also has scaling on her palms This is an allergic reaction to something that has been applied to the patient's hair

DR. C S LIVINGOOD Both Dr Beerman and Dr Whelan are right The patient has a Koebner phenomenon at the sites of her shoulder straps She may have both contact dermatitis and lichen planus

DR MEYER L NIEDELMAN Pityriasis rubra pilaris may have an acute explosive onset, it may start on the scalp and travel to the face I believe that this is a case of pityriasis rubra pilaris with a sudden and acute onset The patient has had no medication and has gone to the beauty shop many times before, with no ill effect The plugs and the involvement of the hairy areas are in accord with that diagnosis

DR D M SIDLICK I do not recall seeing in any reports or textbooks pityriasis rubra pilaris characterized by lichenoid lesions, and, if this is such a case, we shall have to change our concept once again

DR FRED D WEIDMAN There is a condition known as lichen planopilaris, maybe that would reconcile the different diagnoses that have been advanced In the histologic sections it was found that the lichen planus changes do extend down around the hair follicles, making them unduly prominent At the Naval Hospital there was a patient who had a patch of hypertrophic lichen planus on the thigh, and in one there were definite pits, which made me think at first of those which occur when one pulls out a plug from a lesion of Darier's disease These were located at the orifices of hair follicles I would suggest that the patient be examined with respect to a diagnosis of lichen planopilaris, which would bridge the two separate diagnoses advanced

DR LOUIS GOLDSTEIN I thought that lichen planopilaris had to do with the scalp and not with the glabrous parts of the body

DR. HERMAN BEERMAN The typical lesions of lichen planopilaris do occur on the wrists usually

NOTE—Microscopic examination of a biopsy specimen by Dr Fred D Weidman and by Dr Ernest Regertis resulted in a diagnosis of pityriasis rubra pilaris

given In February 1947, dark field-positive primary syphilis was diagnosed at another institution, and the patient was given 2,400,000 units of penicillin According to the patient, the lesion did not heal

DISCUSSION

DR DONALD M PILLSBURY I did the original dark field examination on this patient in February 1928 As the history indicates, for many years thereafter, in spite of what was presumed to be good antisyphilitic treatment, lesions of early syphilis, from which T pallidum was recovered, continued to develop on his skin The patient apparently now has granuloma inguinale, but I would not doubt the capacity for infectious lesions of early syphilis to develop even now, in view of the past history A picture which I cannot get out of my mind in connection with this patient is that of rows on rows of filing cases in the Department of Medicine and Surgery of the Veterans Administration, all containing the records of men treated for syphilis in the Armed Forces Many of these have received penicillin therapy and, in the year 1945 at least, penicillin of very doubtful antisyphilitic potency When one observes relapses and/or reinfections after penicillin therapy and patients such as this one, the enormous potentialities of such patients in terms of the public health are very apparent Syphilis is far from being well controlled, and our methods to this end are still not so effective as they should be

DR DOUGLASS A DECKER, Allentown, Pa This is the first time that I have seen a white patient with granuloma inguinale

DR HERMAN BEERMAN I have seen this patient for nineteen years I can concur in the statement that he had a positive dark field examination in 1928 and that we obtained positive inoculation in rabbits with a portion of his penile lesion in 1934, even in 1934 we thought that he had granuloma inguinale, and he received some injections of antimony potassium tartrate then Every time that Dr Stokes wanted a dark field-positive lesion for teaching purposes he used to say "Get that boy" I think the primary diagnosis now is granuloma inguinale There were Donovan bodies present

FOLLOW-UP NOTE The patient was given 20 Gm of streptomycin intramuscularly in five days (Nov 25 to 30, 1947) The lesions healed promptly, without recurrence to date (October 1949)

A Case for Diagnosis (Senear-Usher Syndrome? Pemphigus Vulgaris?)
Presented by DR CHARLOTTE JORDAN

DETROIT DERMATOLOGICAL SOCIETY

Henry A Brunsting, M D, *Chairman*

Hermann Pinkus, M D, *Recorder*

March 26, 1947

Necrobiosis Lipoidica Presented by DR H J PARKHURST, Toledo, Ohio

K D R, a married woman aged 39, presents on the inner aspect of the lower right shin a large coin-sized morphea-like patch of four years' duration, with sharp borders and some scaling of the surface The ivory-colored center shows telangiectases, and toward the border the tint was violaceous On the dorsum

Scleroderma in an Infant. Presented by DR J. M. SCHILDKRAUT, Trenton, N J.

A B, an infant 1 week of age, has had an eruption on the back since birth Examination shows hard, infiltrated plaques on the upper part of the back, anterior aspect of the chest and the right cheek

DISCUSSION

DR. CARMEN C THOMAS I suggest the diagnosis of subcutaneous fat necrosis of the newborn The lesions were present at birth, after a difficult labor lasting a day and a half, with delivery finally accomplished by forceps The lesions are deep seated, with the periphery beginning to show gradual involution

DR D M SIDLICK Scleroderma in an infant 1 week old would be accompanied by clinical evidence of systemic involvement The tense, edematous skin as well as the distribution and its presence since birth are more in consonance with the diagnosis of scleredema than scleroderma

DR FRED D WEIDMAN I offer an alternative diagnosis of lipophagic granuloma

DR J M SCHILDKRAUT, Trenton, N J Dr Klauder thought that the patient had scleroderma

DR H H PERLMAN I have seen a good many cases of so-called subcutaneous fat necrosis in the newborn The condition is usually described as sclerema neonatorum by many writers (misnomer) The mother stated that she had had an unusually difficult and prolonged labor It is for this reason that trauma should seriously be considered as a causative factor The condition appears a few weeks after birth and invariably disappears spontaneously, usually after a few months Someone mentioned sclerema neonatorum I do not think that this is a case of sclerema neonatorum, because that is a congenital condition or appears soon after birth (usually between the second and tenth day after birth) The condition affects the lower extremities and then spreads to the trunk In sclerema neonatorum, on pressing the affected sites one gets the impression that one is prodding the skin of a cadaver, the skin feels like half-frozen tissue Most patients with such a condition die early The lesions are rather extensive in this case, which is strongly in favor of subcutaneous fat necrosis If this is not a case of subcutaneous fat necrosis, then I would endorse the diagnosis of scleroderma

Reuben Friedman, M D, *Chairman*

Douglass A Decker, M D, *Secretary*

Sept 19, 1947

Multiple Benign Cystic Epithelioma in a Girl Aged Eight Years. Presented by DR LEWIS M JOHNSON, Lancaster, Pa

A Case for Diagnosis (Angioma?). Presented by DR JOHN F WILSON

A J, a white woman aged 49 years, has a group of small red papules in the middle of the flexor surface of the left forearm The color can be pressed from the lesions, and the intervening skin is erythematous In August 1945, the patient had an appendectomy and right oophorectomy for simple ovarian cyst and appendicitis In April 1947, an exploratory laparotomy and transverse colostomy

of the left foot is a cluster of pea-sized brownish erythematous nodules grouped in a circle the size of a large coin These appeared after she had returned from Florida a week ago

Urinalysis and blood sugar studies showed no diabetes, and there was no family history of that disease

DISCUSSION

DR HARTHER KEIM The recent lesion on the left foot and the older one on the right foot look like granuloma annulare I wonder whether the large lesion on the shin is not the same

DR LOREN SHAFFER I agree with Dr Keim that this is a granulomatous process The older lesion is hardly typical of necrobiosis, because of the elevated border The youngest lesion has developed so quickly that it may be erythema diutinum Biopsy is indicated

DR ARTHUR JAMES The margin of the large lesion resembles granuloma annulare, the center looks like necrobiosis lipoidica

DR FELIX PINKUS The lesion looks like granuloma annulare, but everything on the legs below the knees is suggestive of necrobiosis

DR HARTHER KEIM We should keep in mind the case of Dr Belote's in which the disease later turned out to be ulcerating tuberculosis

DR HENRY BRUNSTING One must consider lipid disturbances of other types

DR HOWARD PARKHURST I am sorry that no biopsy could be done The lesion looked more typical when I saw the patient first, several months ago, and this is only the second time I have seen her The appearance of the patch has changed, possibly owing to the roentgen treatment she has received The lesions on the left foot are different, possibly due to insect bites, because she was in Florida, a week ago, when they suddenly appeared

Lupus Erythematosus Limited to the Lips and Buccal Mucosa in a Woman Aged 37, Duration Nine Years Presented by DR H J PARKHURST

Lupus Erythematosus of Mucous Membrane of the Lips and Buccal Mucosa in a Man Aged 37, Duration Eleven Years Presented by DR HENRY A BRUNSTING

Discoid Lupus Erythematosus of the Nose in a Woman Aged 41, Duration Fourteen Years Presented by DR HENRY A BRUNSTING

Two Cases of Congenital Ectodermal Defect (Incomplete) Presented by DR H J PARKHURST

Circumscribed Scleroderma Presented by DR ARTHUR JAMES

Circumscribed Scleroderma of Six Weeks' Duration (Scleredema?) Presented by DR ARTHUR JAMES

Multiple Idiopathic Hemorrhagic Sarcoma of Kaposi Presented by DR HENRY A BRUNSTING

J H, a Negro aged 61, first noticed small tumors on the soles of both feet about 1940 These have progressed to involve the entire right sole and toe and the left instep

were performed for postoperative adhesions and diverticulitis of the middle part of the sigmoid In August 1947, resections of the sigmoid were done for adenocarcinoma with metastasis to the regional lymph nodes The patient noticed a small red spot in the middle of the left forearm a year ago This remained about the same until May 1947 After an exploratory laparotomy the lesion spread, the present eruption has existed for several months

A blood cell count revealed 78 per cent hemoglobin, 4,300,000 erythrocytes and 6,000 leukocytes The urine was normal The Wassermann and Kahn reactions of the blood were negative The blood urea nitrogen was 13 2, plasma proteins 6 15, albumin 4 29 and globulin 1 9

DISCUSSION

DR FRED D WEIDMAN I think that it is necessary to see the sections for the diagnosis They show clearly the structure of a capillary angioma It is not a solitary large tumor, but there are microscopic puncta in the tissues The neoplasm is scattered throughout the section There is a good deal of hyperplasia of the endothelium More of the epithelium seems to comprise the bulk of the lesion than the blood vessels Perhaps that is why the lesion does not appear to be particularly red The patient has had this, I understand, for five years, which would point to the diagnosis of angioma rather than angiosarcoma A general pathologist from the sections might diagnose this as an angioendothelioma proliferating into the surrounding tissue, but dermatologists know that there are other lesions, such as granuloma pyogenicum and dermatofibromas, which appear to be infiltrative and yet do not have the neoplastic property of a true malignant condition I should say that these are capillary angiomas rather than angiosarcomas

Pityriasis Rosea? Neurofibromatosis Presented by DR EVAN B HUME

DISCUSSION

DR EVAN B HUME Why is neurofibromatosis aggravated by pregnancy?

DR BERTRAM SHAFFER Many conditions either develop or become aggravated during pregnancy Cutaneous tags, various pigmentations, verruca senilis and von Recklinghausen's disease belong to this group of eruptions

DR SIGMUND S GREENBAUM I offer the diagnosis of a mixed type of anetoderma None of the lesions look like pityriasis rosea The larger lesions resemble Schweninger-Buzzi disease

DR REUBEN FRIEDMAN I agree with the diagnosis of pityriasis rosea and von Recklinghausen's disease Dr Cipollaro of New York is opposed to biopsies in frank cases of neurofibromatosis, stating that in 13 per cent of the cases sarcoma develops at the site of the biopsy

Lupus Erythematosus, Scleroderma (Sclerodactylia), Raynaud's Disease, Sarcoidosis (Boeck's?) Presented by DR LEWIS M JOHNSON, Lancaster, Pa

Keratoses of the Palms and Soles (Chronic) (Caused by Arsenic?), Pigmentation (Generalized) (Caused by Arsenic?), Dermatitis (Atopic) of the Hands, Forearms, Ankles and Popliteal Areas (Chronic), Cirrhosis (Portal) of the Liver (Chronic) (Cause Undetermined) Presented by DR LESLIE NICHOLAS and (by invitation) CAPTAIN A FRISKEL

Examination disclosed numerous pea-sized and larger round, firm nodules, pink to brownish, distributed over the soles and toes of both feet Some of the lesions, of a verrucous nature, have dropped out, leaving a pea-sized excavation

Results of laboratory examinations, including a complete blood cell count, differential count, urinalysis, serologic test for syphilis and roentgenogram of the chest, were all within normal limits A roentgenogram of the feet showed some disuse atrophy but no bone destruction A culture from the lesions of the feet disclosed gram-positive diplococci but no fungi Histologic examination disclosed a sarcomatous stage of multiple hemorrhagic pigmented sarcoma (Kaposi)

In addition to topical therapy, the patient received potassium iodide orally, and between Feb 11 and 19, 1947, he received seven roentgen treatments to the lateral surfaces of each foot (200 kilovolts, 50 cm distance, 4 mm of copper filter) for a total of 1,050 r to each area There was considerable improvement following radiation therapy

DISCUSSION

DR ARTHUR JAMES I saw this man seven years ago His feet were swollen and had draining sinuses Biopsy showed blastomycosis He improved very much with potassium iodide therapy

DR FELIX PINKUS Today I made a clinical diagnosis of Kaposi sarcoma, and the histologic picture seems to confirm this

DR HOWARD PARKHURST The lesions now look like the idiopathic sarcoma of Kaposi, but eight months ago the condition resembled mycetoma The sinuses which were present then cleared up with moist packs of potassium permanganate solution More recently, after roentgen treatment, the nodules have subsided

DR THOMAS MILLER I agree with the diagnosis of Kaposi sarcoma The most plausible explanation would seem to be that it has recently developed on the background of an older, infectious process

DR HENRY A BRUNSTING I believe that the clinical and histologic picture is consistent with the diagnosis of Kaposi sarcoma There has been considerable improvement in the clinical picture in the month since radiation therapy was administered

Porokeratosis (Mibelli) of the Thumb of a 7 Year Old Girl Presented by DR H J PARKHURST and DR HENRY A BRUNSTING

Bright Red Nodular Tertiary Syphilid on the Thigh, Duration Eight Years Presented by DR HENRY A BRUNSTING

Tuberculosis of the Skin. Presented by DR H A. LUSCOMB for DR FRANK C KNOWLES

T C a Negro woman aged 21 years, presents a generalized, lichenoid, umbilicated, papular eruption with condylomata lata on the external genitalia The patient was admitted to the clinic in January 1947, with a history of an eruption of two months' duration

The Wassermann and Kahn reactions of the blood were strongly positive A blood cell count and the results of urinalysis were normal The serum calcium was 11 2 Roentgenograms showed the chest, hands and feet normal The result of a tuberculin test performed on April 1 with purified protein derivative (first and second test dilutions) was negative

The diagnosis from biopsy was tuberculosis

Antisyphilitic treatment with oxophenarsine hydrochloride was begun on Jan 17, 1947 The condylomata disappeared, but the rest of the eruption remained the same after three months' treatment Calciferol (vitamin D_2) therapy, 100,000 units daily, was started on May 31 and continued to the present time The eruption on the face had disappeared in six weeks The rest of the eruption has slowly improved

DISCUSSION

DR D M SIDLICK Only the microscopic evidence is in favor of tuberculosis of the skin, and I do not believe that one can make a diagnosis merely on the basis of the histologic picture The clinical evidence favors syphilis, and this is a macular atrophy following secondary syphilis

DR FRED D WEIDMAN This might be a case of sarcoid in the form that occurs in the American Negro, which responds to vitamin D_2 therapy The sections suggest sarcoid, although there are many lymphocytes, there are no giant cells The patient is anergic, but the other lesions, such as the bone changes, appear not to be present The disease is, however, in an early stage, and I think that the case should be watched because it may be one of sarcoid of the American Negro, which Dr Michelson thinks might be different from sarcoid of Boeck

DR C C THOMAS I have seen at least three examples of what appeared to be papular secondary syphilis which on further examination and failure to respond to antisyphilitic therapy turned out to be sarcoid I suggest a lymph node biopsy

Purpura Annularis Telangiectodes (?) Improved Following Treatment with Rutin and Ascorbic Acid Presented by DR SIGMUND S GREENBAUM

Follow-Up Report Presented by DR J M SCHILDKRAUT, Trenton, Pa

Some time ago I reported an extensive case of plantar warts—one of the worst I had ever seen The boy had an extensive case of fused warts on the whole anterior part of the foot and scattered warts on the heel and toes, he also had warts on his hands He had received roentgen rays, bismuth preparations and other medicaments without effect I gave him a course of bismuth injections and advised that he soak his foot, at the suggestion of Dr Livingood, in 3 per cent formaldehyde, and the condition cleared up

News and Comment

GENERAL NEWS

Third Annual Clinical Session of the American Medical Association — The Third Annual Clinical Session of the American Medical Association will be held in Washington, D C, December 6 to 9

The Clinical Session will provide a full scale scientific program specifically designed for the general practitioner Outstanding physicians will discuss such subjects as diabetes, pediatrics, laboratory diagnosis, physical medicine and rehabilitation, arthritis, dermatology, diagnosis by means of the roentgen rays, cancer and poliomyelitis Coordinated with this outstanding scientific program will be approximately one hundred scientific exhibits which will present original work on the subjects discussed

The newest offerings of one hundred and twenty-five manufacturing firms will comprise the Technical Exhibition Here will be found the latest developments in scientific medical research, drugs and equipment

Televised surgical and clinical procedures, similar to those shown in color at the Annual Session of the American Medical Association in Atlantic City last June, will be presented at the Washington meeting The demonstrations will originate in the Johns Hopkins Hospital and will be shown on screens in the Armory The television schedule will be spread over four days

The House of Delegates will meet at the Hotel Statler during this session One of the first orders of business will be the annual selection of the general practitioner who has made an exceptional contribution of service to his community

An entertainment program for attending physicians and their wives is planned The highlight of this program will occur on Wednesday evening, December 7, when Philip Morris will originate its "This Is Your Life" broadcast from the Hotel Statler The radio program will be followed by a stage show, in which outstanding stars will participate

Blanks for hotel reservations and advance registrations may be found in *The Journal of the American Medical Association*

Reuben Friedman, M D, *Chairman*

Douglass A Decker, M D, *Secretary*

Oct 17, 1947

A Case for Diagnosis (Psychosomatic Dermatitis? Dermatitis Herpetiformis?) Presented by DR REUBEN FRIEDMAN and (by invitation) DR CONRAD STRITZLER and DR JOHN B ROXBY JR

Xanthoma Eruptivum Secondary to Lipid Nephrosis Presented by DR REUBEN FRIEDMAN and (by invitation) DR WALDO E NELSON, DR CONRAD STRITZLER and DR JOHN B ROXBY JR

Combined Simple and Cavernous Angioma Presented by DR MEYER L NIEDELMAN

D A, a white girl aged 2 months, presents over the entire left side of the face an angioma cavernosum It is bright red, and the prominence of the swelling lies over the parotid gland There are numerous both raised and flat simple hemangiomas scattered over the right side of the face and neck On the lower lip there is a similar lesion

A small red area developed in front of the left ear at 2 weeks of age Another lesion formed on the lower lip, then gradually new areas developed over the left and right sides of the face and neck The patient was seen two days ago, and arrangements are being made to treat the lesions with radium

DISCUSSION

CAPT R L GILMAN, U S N This patient should be treated with sclerosing injections or solid carbon dioxide I would not use radium or roentgen rays

DR MEYER L NIEDELMAN I am afraid to use sclerosing solutions about the scalp and face because of possible thrombosis of a cerebral vessel At a meeting of the American Academy of Dermatology and Syphilology a few years ago a case was reported in which death of an infant was due to the injection of a sclerosing solution for an angioma of the face I believe the cosmetic result would be poor with solid carbon dioxide, and this substance is ineffective in the cavernous type I shall use radium, and I am sure a regression of the angioma will take place

DR H E TWINING The more rapid the growth, the greater the response one gets from radium or roentgen rays

DR M H SAMITZ I suggest that a roentgenogram be taken of the face to see whether there is any involvement of bone

DR THOMAS BUTTERWORTH, Reading, Pa Frequently extensive hemangiomas occurring in the trigeminal area are accompanied with hemangiomas of the cerebral cortex, and in treating them with roentgen rays one exposes oneself to a medicolegal proceeding If cerebral lesions develop later, the patient's parents may ascribe them to the treatment given earlier At the age of 12 or 14 the angioma on the cortex of the brain may become calcified and can be demonstrated by roentgenogram

DR HERMAN BEERMAN What is "simple" angioma?

DR MEYER L NIEDELMAN There are two types present in this infant the small, flat type, which is simple, and the elevated, doughy, vascular type, which is cavernous

Book Reviews

Malattie cutanee e veneree ed alterazioni oculari By G Sala and P Noto, with prefaces by A Grosti and B Alajmo Pp 410 Palermo, Italy S F Flaccovio, 1948

This book, which is probably the most comprehensive monograph on the subject, is the combined work of the ophthalmologist, G Sala, and the dermatologist, P Noto, both of the University of Palermo, Italy The authors discuss, in parallel articles, the embryology of the skin and of the eye and all dermatoses and venereal diseases which may affect the eye and the lids The book contains a vast amount of factual, mostly clinical and often original, material in connection with a rather large bibliography

There are some shortcomings which should be corrected in a new edition There are no illustrations and no alphabetic index, and the paper is poor, probably because of postwar difficulties It would be to the advantage of the book if the authors would agree on more rigid editing It seems out of proportion to write a page or more on the dermatologic aspects of lichen planus and other dermatoses and then to mention, in a few lines, the rarity of participation of the eyelids The spelling of foreign names and titles of publications, especially in the German references, is poor Of greater importance than errors of this kind is the omission of discussion of the work of Brunsting and Sheard and others on the high threshold level of dark adaptation in pityriasis rubra pilaris However, these shortcomings should not distract from the great value of the work as a modern reference book

Of interest is the observation of the relative frequency of dermatogenous cataract in cases of generalized psoriasis In this connection, it may be mentioned that the authors estimate that cataract develops in 10 per cent of the patients with neurodermatitis (atopic dermatitis) This percentage appears to be a higher one than is observed in America, and the discussion should prompt a study of the eye in a large number of American cases

An Introduction to Dermatology By J H Percival, M D Eleventh edition Price, $9 Pp 349 Baltimore Williams and Wilkins Company, 1947

In general this is an excellent, small, yet complete book, in which the author well meets the difficult problem of attempting to cover a large and complex field briefly The material is well organized and clearly presented and indicates logical thinking throughout There are sufficient good colored illustrations to help the presentation greatly

Though brevity and a superficial approach are necessary in a book of this type, there seems to be an insufficient attempt made to link dermatology to the whole of medicine Mention of the more serious general involvement of the body of many dermatoses is omitted in the discussion of some conditions and but briefly touched on in others

American readers, although likely agreeing in general with the material presented, will undoubtedly have varying opinions regarding certain specific ideas expressed Among such controversial points, the following ones might be mentioned that the Senear-Usher syndrome is a type of generalized lupus erythematosus and that this syndrome is identical with pemphigus foliaceus, that dermatitis herpetiformis "may imperceptibly change its character to that of pemphigus," that twelve hours is sufficient time for patch testing and that "if there is no reaction, any suspicion of the substance used for the test may be dismissed"

so far are unknown to us Treatment with penicillin and sulfonamide drugs have had little effect on the course of the disease

The nodes have a tendency to mat together The ulcers are variable in size and shape, from 2 to 5 cm in diameter, and have a soft undermining edge and irregular granulating bases, well vascularized Some of the ulcers have appeared over regions where large lymph nodes are not usually present On the roentgenogram of the skull there is an irregular, oval dehiscence of the right parietal bone under one of the tender swellings The spleen is palpable The liver is felt at the costal margin

The axillary lymph node, seen on Jan 30, 1947, was a large moderately firm node of a peculiar red-brown The microscopic sections showed a very extensive obliteration of the normal architecture, although small remnants of cortical follicles and cords filled with lymphocytes remain These are widely separated and are missing from some parts of the node Instead one finds sheets of large acidophilic or pale nonfoamy macrophages, which seem to have filled in the sinuses as well as the parenchyma Scattered in great abundance between them are eosinophils and smaller dark cells which are presumably lymphocytes In some regions the cells with dark nuclei look more like normoblasts The histiocytes or macrophages frequently have lobulated nuclei, and sometimes they contain two or more discrete nuclei Neither in their cytoplasm nor in their nuclear form do they resemble Reed-Sternberg cells They do not possess distinct nuclei as shown in Mallory connective tissue stain, there is great fibrous thickening of the capsule and decided fibrosis of some of the cell-filled lymphatic sinuses Fibrous tissue is especially dense around the blood vessels of hilar portion of the node Evident in Mallory stain more clearly than in hematoxylin and eosin is the presence of clefts or small vacuoles of the cytoplasm of the large macrophages However, the appearance is quite different from that seen in the large cells of Gaucher's disease, in Niemann-Pick's disease or in Hand-Schüller-Christian's xanthomatosis Stains for gram-positive and acid-fast bacteria were entirely negative Sudan stain reveals an occasional macrophage containing recognizable septums A very small amount of this lipid is antisotrophic

The scraping of the sinus tract consists of multiple bits of granulation tissue and fragments of skin which show changes similar to those of the lymph nodes In the section of the skin the eosinophils are less prominent Plasma cells and large mononuclear cells are present The disease has been diagnosed once as tuberculosis by smear examination, and at another time as Hodgkin's disease by lymph node examination

In our laboratory tests, culture of the exudate on blood agar and Sabouraud's medium showed Staphylococcus albus The acid-fast stain was repeatedly negative Blood culture was negative White rat and guinea pig inoculations were repeatedly negative, results of the tuberculin patch test, blastomycin test, histoplasmin skin tests and purified protein derivative tests were all negative The Kahn reaction of the blood was negative Sternal puncture showed the myeloblast-erythroblast ratio to be elevated Other observations were sedimentation rate 41 mm in 1 hour, leukocytes 12,000, hemoglobin 12 Gm, erythrocytes 4,400,000, poloymorphonuclear cells 72 per cent, lymphocytes 26 per cent, eosinophils 2 per cent, hematocrit 41 and blood lipids 787

The histologic section from a lymph node presented a very unusual appearance which did not resemble any lymph node previously studied in our laboratories Certainly tuberculosis and Hodgkin's disease in their usual forms can be excluded On anatomic evidence at present, we have no clue as to whether this peculiar

granulomatous condition is an infection or is caused by a metabolic anomaly It more closely resembles the tissue reaction seen in eosinophilic granuloma of bone than any other condition known to us

DISCUSSION

DR CARL W LAYMON, Minneapolis There is not a great deal known about eosinophilic granuloma of the skin, since not more than a dozen cases have been reported and in those cases the diagnosis was doubtful The disease has been reported in nodules or plaques which brings up the interesting question as to whether cutaneous eosinophilic granuloma is related to eosinophilic granuloma in the lung and other organs That brings up a possible relation to Christian's disease I believe that all of these diseases are part of the same toxic process and that this occurs as a fatal type and the Christian type occurs as a more benign disease Cutaneous eosinophilic granuloma and eosinophilic granuloma of the bone are part of the same process Last April, at the meeting in Detroit, Dr Curtis showed a patient with eosinophilic granuloma of the bone with cutaneous lesions

DR A C CURTIS, Ann Arbor Experience in 1 case does not make one an authority The patient that Dr Laymon mentioned had plaquelike lesions on the vulva and one lesion on the scalp, with a destructive process in the bone of the mastoid and in the crest of the ilium The lesions were plaquelike and very red Our attention was called to them because of the redness They promptly disappeared with a minimal amount of low voltage roentgen rays, as did the destructive lesions in the bone As I looked through the records to see whether any studies had been made, it occurred to me that this might be a disseminated sporotrichosis

DR STEPHEN ROTHMAN The diagnosis of eosinophilic granuloma was first suggested by our pathologist, Dr E M Humphreys I realize that these cutaneous lesions have not been reported in the literature It does not agree with any description published in the literature It reminded me of Niemann-Pick's disease, but the pathologist said that it was not Clinically it was typical scrofuloderma Extensive examinations were made for fungi The patient was seen in several departments I think that we can by now exclude tuberculosis and mycosis

Calcinosis of the Elbows Presented by DR DAVID V OMENS and (by invitation) DR HAROLD D OMENS

Leukoplakia, Sublingual (White Sponge Nevus?) Presented by MAURICE OPPENHEIM and (by invitation) DR WILLIAM A YACULLO

Pityriasis Rubra Pilaris in a Five Year Old Presented by DR MARCUS R CARO and (by invitation) DR LAURENCE L PALITZ

Parapsoriasis Guttata, with Unusually Small Lesions Presented by DR EDWARD A OLIVER and (by invitation) DR E LORANT and DR A B HENNINGSEN

A Case for Diagnosis (Psoriasis? Lupus Erythematosus?) Presented by DR ALBERT H SLEPYAN (by invitation)

Archives of Dermatology and Syphilology

VOLUME 60 NOVEMBER 1949—PART II NUMBER 5

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Society Transactions

ATLANTIC DERMATOLOGICAL CONFERENCE

David Bloom, M D, and Eugene F Traub, M D, *Chairmen*

Wilbert Sachs, M D, and George M Lewis, M D, *Secretaries*

Manhattan and New York Dermatological Societies

March 8, 1947

Cosmetic Repair (Surgical) of Lupus Erythematosus Hypertrophicus et Profundus. Presented by DR SAMUEL M PECK

E B, a housewife aged 40, is presented from Mount Sinai Hospital, New York, with an eruption which appeared after exposure to sun and which has been present since 1925 The patient has been under observation since 1926 She has received a great deal of therapy, including treatment with gold and bismuth preparations, cobra venom and other remedies, but finally improved with administration of suramin sodium (naphuride sodium®) Subcutaneous infiltrations appeared in 1938 With improvement, the infiltrations disappeared, leaving atrophic areas resulting in cosmetic defects

There are still a few areas of activity on the face and scalp consisting of circumscribed patches of atrophy and telangiectasia The sites of the defects have been filled in by means of skin grafts

The patient has been kept practically free of lesions by injections of naphuride® The dosage was 100 mg with increase at each injection until a maximum dosage of 300 mg was given All injections were intramuscular and given once a week From October 1945 until the present she has received several courses of this drug the first consisting of eleven injections and the second of eight The third course, which comprised seven injections, was begun in June 1946

The reason for presenting the case was the great loss of subcutaneous fat at the sites of the previous infiltrations, with scarring over the flush areas of the cheeks A repair, consisting of dermal grafts, was performed by Dr Michael L Lewin Only the dermal component of the graft was utilized in order to limit shrinkage as much as possible

DISCUSSION

DR FRANCIS P MCCARTHY, Boston May I ask Dr Peck whether, on the basis of its use in 40 cases, he feels that this drug is safe for use by the medical profession? It seems to me that it is a toxic drug, capable of producing a renal irritation, as evidenced by casts and albuminuria Personally, I would prefer to use a less dangerous remedy

DR MAURICE J COSTELLO I have used naphuride® in the treatment of lupus erythematosus in 6 cases, with spectacularly good results in 3 of them, in half of the patients severe toxic reactions developed and the use of the drug had to be discontinued One patient had disturbance of vision, 2 had swelling of the hands and feet accompanied with intense pruritus, others had pain and swelling of the

Dark field examinations of the lesions on the tongue and arm gave negative results, as did the Mazzini reaction of the blood A complete blood count, examination of the urine and roentgenograms of the lungs revealed no abnormalities

Biopsy of the lesion on the arm, done at Bellevue Hospital, showed a nonspecific granuloma with epithelioid cells, plasma cells and lymphocytes

Material from the lesion on the left side of the dorsum of the tongue was examined by Dr Fred D Weidman, who reported the lesion to be syphilis or oriental sore He found the epidermis to be enormously acanthotic and parakeratotic Although its squamous cells were greatly swollen, there was no evidence of neoplastic activity, even at the basement membrane There the basal cells had undergone metaplasia into squamous forms There, too, many of the inflammatory infiltrative cells of the corium were infiltrating the epidermis A rather heavy infiltration of inflammatory round cells lay immediately below the epidermis It crowded the papillae but did not extend farther than the subpapillary plexus of vessels The cells were distributed diffusely, and although lymphocytes were dominant, there was a large intermixture of elongated nuclei which were interpreted as epithelioids However, none of them was congregated into individual foci in such a way as to constitute miliary granulomas There were numerous other elongated nuclei which were clearly those of histiocytes, but they were readily distinguishable from the plumper epithelioid ones

The significant features in the diagnosis resided in the epithelioid cells Such cells do appear in the lesions of oriental sore, but in the absence of the specific organisms the epithelioids could reasonably be those of syphilis or tuberculosis, the diffuse distribution would point more toward syphilis The protozoa were not recognizable in these sections

DISCUSSION

Dr Fred Weidman, Philadelphia The solitary item of significance in the histologic picture is the presence of epithelioid cells, which are not gathered into foci to indicate definite miliary granulomas of either syphilis or tuberculosis In other words, it is a diffuse reaction such as occurs in pneumonia alba In such a situation it is necessary to resort to methods for the identification of the parasite itself I might say that the only time recently that I have seen the Leishman-Donovan body in sections was at Dr Lloyd W Ketron's laboratory, but that is unusual A much more preferable method of demonstrating the parasites is by means of smears, so I should say that if the pursuit of the Leishman-Donovan body is to be continued, that is the method of choice After seeing the patient today, I do not think the lesion could be that of leishmaniasis, as the infiltration of the tongue is not particularly heavy It is rather superficial for that disease, and leishmaniasis is usually more suppurative, as I recall it, there is no evidence of pus in the sections After seeing the patient again, I do not think it is likely to be syphilis, which I intimated in the histologic reports I was swayed by the fact that the infiltration is diffuse

Dr Clarence S Livingood, Philadelphia Several years ago I had an opportunity to observe a rather large number of patients with cutaneous leishmaniasis, and this case certainly does not correspond with any of those which I have seen I gathered that the type of ulcer which the patient had was not characteristic of that disease According to the information which I obtained from him, his stay abroad was entirely confined to Greece, and as far as I know leishmaniasis does not occur in that country

Dr Bernard Appel, Lynn, Mass The lesions on the lips and in the mouth are, in my opinion, consistent with lupus erythematosus It is not unusual, in my experience, to find lesions on the lips which in the early stages resemble those of

joints and in 1 the urine indicated renal irritation I believe that the drug is to be used with great caution It is effective, but it should be given only in the refractory, severe cases

DR. GEORGE C ANDREWS I agree with Dr Costello I think Dr Peck has had more experience with germanin in the treatment of lupus erythematosus than anybody in this city, and he can do things with it, perhaps, that the average physician cannot do I agree fully with his remarks, except that I think he should be a little more careful in explaining how toxic naphuride® is Severe anemia, hepatitis and nephritis occur from its use The total dose must be kept under 1 Gm for a long period I feel, as Dr Costello does, that it is an extremely toxic drug I no longer use it in cases of pemphigus, although I do use it for lupus erythematosus of the discoid type in small doses of 100 mg once a week for six or eight weeks If the patient is carefully watched, such doses are fairly safe In some cases fine results are obtained, and in others it does no good

A Case for Diagnosis (Lymphoblastoma? Pemphigus? Dermatitis Herpetiformis?) Presented by DR. ISADORE ROSEN

E A, a woman aged 70, had an eruption of four years' duration This began as vesicular plaques on the wrists and hands After roentgen ray treatment the eruption disappeared, but it soon recurred on the face, chest and extremities Since then there have been complete remissions and also exacerbations of varying degree, the patient having to be hospitalized on several occasions

The eruption during the past few years has been generalized and has consisted of grouped and fused lesions of vesicular character On the face and extremities infiltration has been frequently observed, and at times the lesions have been oozing or covered with scales At other times they have been annular, with central vesicular crusting, and have closely resembled pityriasis rosea In August 1946, shortly before her hospitalization, almost the entire surface of the skin was involved, except for the palms and soles At that time the patient presented on the face, neck and chest diffuse dull erythema, edema and exfoliation The rest of the body showed rounded erythematous lesions from 2 to 7 cm in diameter, with a scaly collar just inside the erythematous border In some areas there were flattened bullae containing clear fluid During the patient's stay in the hospital new bullae appeared from time to time

The Wassermann and Kahn reactions of the blood were negative Frequent blood counts showed leukocytosis, with a count which at times reached a figure of about 18,000, and a high eosinophil count, on some occasions as much as 27 per cent Roentgenograms of the lungs revealed moderate central thickening of the lymphomatous type, with clear peripheral lung fields A roentgenogram of the spine showed localized hypertrophic changes of the lower cervical area.

Patch tests with 30 per cent potassium iodide and potassium bromide ointment gave a strongly positive reaction Chemical studies of the blood, including determination of the nonprotein nitrogen, total protein, albumin, globulin, icterus index, calcium, inorganic phosphate and sugar, showed normal figures The last examination of the erythrocyte sedimentation rate during an exacerbation showed 93 mm per hour The basal metabolic rate was within normal limits

Four biopsies taken at different times were reported to show (1) chronic dermatitis, (2) neurodermatitic reaction, (3) psoriasiform dermatitis, and (4) pemphigus The description of the last slide was as follows "There is an

lichen planus clinically because of the white reticulation and their limitation to the vermillion of the lip With the progress of the disease, however, the lesions become more characteristic as they extend to the glabrous skin I anticipate that that is what will happen in this case Furthermore, I have not found that lichen planus produces such extensive and persistent ulceration of the tongue when it does occur there, that is to say, this picture is more consistent with lupus erythematosus If it actually is lupus erythematosus, it is also my opinion that it is likely to be extremely resistant to treatment and that the prognosis should be guarded

DR FRANCIS P MCCARTHY, Boston Dr Weidman, does the lesion on the tongue show epithelioid tissue?

DR FRED WEIDMAN, Philadelphia Yes

DR FRANCIS P MCCARTHY Do we get this reaction in lupus erythematosus?

DR FRED WEIDMAN No

DR MAURICE J COSTELLO The question of tuberculosis of the tongue also came up, but roentgenograms showed the chest to be normal We have seen patients who had both lichen planus and lupus erythematosus simultaneously I think the lesions on the lower lip suggest lichen planus and am inclined to agree that the lesion on the tongue is lupus erythematosus or lichen planus clinically

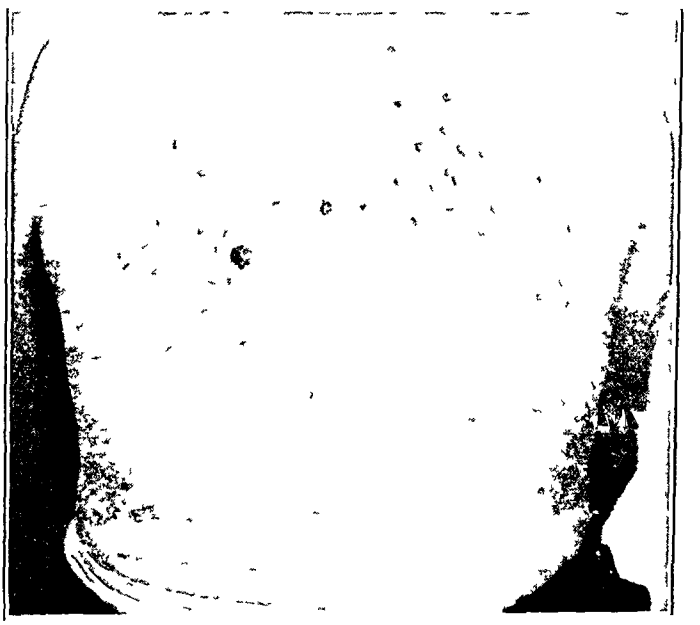


Fig 7—Lesions of leiomyoma

Leiomyoma Presented by DR ANTHONY C CIPOLLARO

P P, a man aged 52, is presented from the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, with an eruption of fifteen years' duration which has not changed essentially in the past twelve years

In the scapular region there is a symmetric eruption of slightly reddish, mostly oval, elongated and spherical infiltrated, firm, nodular lesions which are arranged in the lines of cleavage There is a moderate number of similar but smaller and less indurated lesions in the lower lumbar and gluteal region Some of the lesions are tender to pressure The patient complains of severe pain in the region of the eruption during cold weather

intraepidermal cavity with numerous eosinophils In the upper cutis the vessels are dilated and show swelling of the intima There is a diffuse infiltration of small round cells, wandering connective tissue cells, numerous eosinophils and occasional plasma cells"

Treatment has consisted of superficial irradiation, injections of arsenic and liver extract and blood and plasma transfusions Sulfapyridine was given, but its use had to be discontinued because of nausea and vomiting The last treatment given in the hospital and being continued in the clinic is administration of

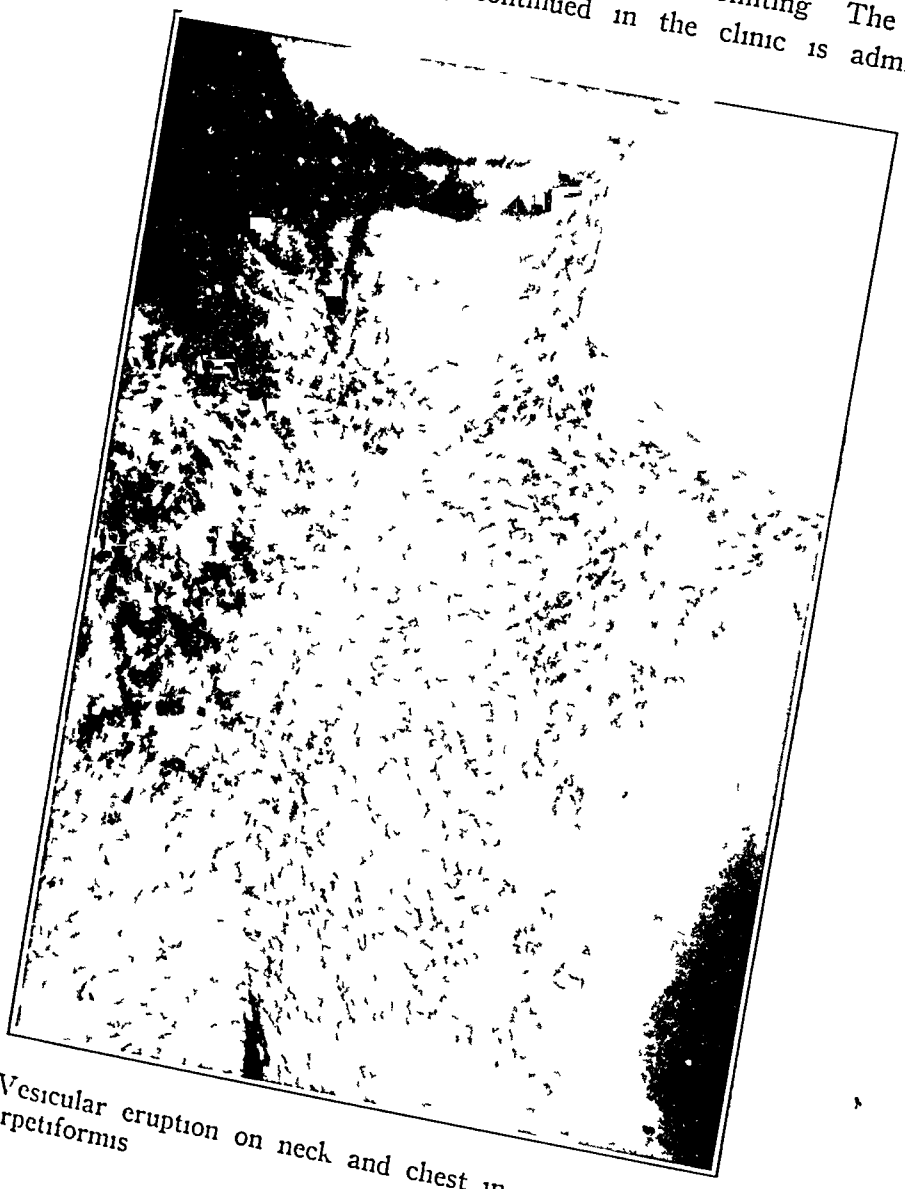


Fig 1—Vesicular eruption on neck and chest in a woman with questionable dermatitis herpetiformis

mphuride® in a dose of 0 25 Gm intramuscularly twice a week This seems to have benefited the patient

DISCUSSION

DR FRANCIS A ELLIS, Baltimore Nausea is not a contraindication to the administration of sulfapyridine We have had severe cases in which we continued to use the drug in spite of nausea and vomiting, and even though the dosage was decreased, good results were obtained in three or four weeks



Fig 8—Photomicrograph showing leiomyomatous changes

: WILBERT SACHS This patient has had long-standing dermatosis, and
:rimposed pemphigus developed I believe that the underlying dermatosis is
nct dermatologic entity that has never before been described I have now
bout 6 such cases, and the microscopic picture is always the same There
eurodermatitic reaction, with a focal cellular infiltration of plasma cells
rocess suggests an exudative discoid and lichenoid dermatosis on the one
nd a mycosis fungoides on the other Yet it is neither of these diseases but
ite entity falling somewhere between both Clinically these patients may
nacules, papules, nodules or patches This patient also has pemphigus,
ly due to a toxic reaction

WALTER F LEVER, Boston The cutaneous lesions are eczematous in
It is possible that the disease will turn out to be mycosis fungoides
ntly in the prefungoid state of mycosis fungoides it is impossible to find
histologic sections atypical cells which would establish the diagnosis of
; fungoides Instead, only banal inflammatory changes are present In
to a diagnosis of pemphigus, I think that is a disease entity and does not
as a toxic reaction secondary to another dermatosis I would not dare
.e a diagnosis of pemphigus on histologic grounds alone, except in some
of pemphigus vegetans Bullae may occur as an unspecific reaction, both
matous cutaneous disorders and in mycosis fungoides

WILBERT SACHS I did not intend to imply that this was a case of mycosis
les In fact, I believe that disease will never develop in the patient This
the proper time to discuss the differentiation between dermatitis herpeti-
and pemphigus I am not convinced that we know what pemphigus is,
the lesions of that disease are toxic bullous manifestations There are
characteristics on which a diagnosis of pemphigus can be made micro-
lly

GERALD F MACHACEK We have had similar problems at the Presby-
Hospital in which the diagnosis was uncertain The lesions were pemphigoid
e thought to be those of Duhring's disease, and treatment with sulfapyridine
ied and found wanting One such case was presented before the New
Academy of Medicine last Tuesday Dr Vero found that the lesions in
ise and in another disappeared with large doses of vitamin A Perhaps
)sen has already tried that form of therapy

ISADORE ROSEN This patient has been under observation for more than
ears The only subjective symptom has been intense itching, and her
physical condition has never been impaired I am of the opinion that this
eruption is probably due to the effects of treatment over many months

oderma Vasculare Atrophicans with the Histologic Picture of ycosis Fungoides Presented by DR DAVID BLOOM

itis Factitia Dystrophy of the Nails and Keloids of the Palms d Soles Presented by DR GEORGE C ANDREWS

C F, a widow aged 66 from the Roosevelt Hospital, has arteriosclerotic disease, diverticulosis of the colon and hypertrophic arthritis Her psychi-tatus has not yet been determined

Routine examination of the blood and urine gave normal results

Biopsy of a nodular lesion was reported previously to show neuroma Recently another biopsy was reported as showing leiomyoma

Unfiltered roentgen irradiation seems to have alleviated the pain of which the patient has complained

DISCUSSION

DR WILBERT SACHS I made both diagnoses I feel that in regard to multiple small lesions for which the diagnoses of both neuroma and leiomyoma are suggested it is possible that it is not a single, distinct type of tumor but a combination of both Of course it is often difficult to differentiate between neuroma and leiomyoma In this case we did some special stains on the first section and these showed a neuroma On the second section it was not necessary to do any special stains since there was a classic picture of leiomyoma

Pityriasis Rubra Pilaris Uninfluenced by Treatment with Vitamin A Presented by DR E W ABRAMOWITZ

Ragweed Dermatitis Presented by DR MAX SCHEER

P B, a man aged 65, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital He loads Pepsi-Cola bottles as an occupation He was in good health and free from any cutaneous disease until September 1936, when he walked through some lots in Astoria, N Y, without stockings A vesicular eruption appeared on the dorsa of the feet and legs which was at first called eruption from poison ivy and which lasted five months It recurred in September 1937, when it was slight on the feet and legs, mild on the face, hands and forearms and severe on the scrotum The eruption then became perennial, with exacerbations from September to May June and July are the most comfortable months for the patient

There is a thickened, lichenified eruption on the face and forearms The eruption stops rather abruptly on the upper third of his forehead, which is protected by his hat

Reactions to patch tests with oleoresins of short ragweed, cocklebur, sheep sorrel, Kentucky blue grass, red top, poison ivy, orchard grass and timothy were positive Patch tests with the protein extracts of trees, grasses and weeds showed a positive reaction only to oak Scratch tests with these protein extracts gave negative results

The histologic picture was that of a contact type of eczema

No specific treatment has been given as yet The patient has been receiving eight 50 mg tablets of tripelennamine hydrochloride (pyribenzamine®) daily, with only slight alleviation of the itching

DISCUSSION

DR JOSEPH MULLER, Worcester, Mass From the appearance I would be likely to believe that it is a ragweed dermatitis, but, on looking at the calendar and the patient, I just cannot accept that diagnosis After all, ragweed dermatitis is nothing else but a contact dermatitis, and the patient has certainly not been exposed to ragweed for a long time The fact that the reactions to patch tests were positive means nothing I think the patient has at some time had contact dermatitis If ragweed caused the trouble, it should have started in the fall and be over by now

In 1935 the patient was told that she had a fungus infection of the finger nails, which she felt was the reason for her various functional and organic disturbances Since that time she has scraped her palms, soles and finger nails daily in order to "rid her system of disease"

There is almost complete absence of the finger nails and toe nails On the palms and soles are deep, red, linear, thickened areas On the hands, these extend over the palmar surfaces of the fingers

The Kline and Mazzini reactions of the blood are negative The urine is normal, and a complete blood count shows a moderate hypochromic anemia The basal metabolic rate is —4 per cent

Moniliasis Presented by Dr George C Andrews

R V, a girl aged 9, is presented from the Vanderbilt Clinic She was normal and healthy at birth and was well until the age of 2, when "double pneumonia" developed After this she remained underweight and had recurrent furunculosis which continued until the onset of the present illness In August 1943, when the patient was first seen, there was an eruption involving the scalp, mouth, nails and skin which had appeared ten months previously The patient had been hospitalized elsewhere, without improvement

On admission in 1943 the child appeared malnourished Purulent crusted lesions were present on the scalp The mucous membranes were covered with a grayish exudate, the nails were thickened, and many poorly limited, scaling, erythematous lesions were present on the shoulders

Extensive studies have been carried out in the three and one-half year period, only the pertinent findings are presented Repeated cultures of material from the scalp, skin, nails, mouth, sputum and feces were positive for Candida albicans Roentgenograms of the gastrointestinal tract in 1945 showed disturbed function of the ileum In 1946, agglutination of the blood serum for C albicans was positive in a dilution of 1 128

Examination of tissue from the back revealed intraepidermal pustules, with a leukocytic infiltrate in the pars papillaris of the corium

Locally, various preparations, including sulfur, sodium perborate, sodium propionate and gentian violet, have been used Crude liver extract multiple vitamin preparations, Candida vaccine and antiserum were used systemically In 1945, during a nine week period of hospitalization, a protoanemonin antibiotic was administered locally and orally Since July 1946 treatment has included iodine solution locally and strong solution of iodine with folic acid by mouth Recently there has been slight improvement in the cutaneous lesions, although the scalp, mucous membranes and nails are unchanged

DISCUSSION

Dr George C Andrews I have always believed in the use of iodine for moniliasis, and this case is presented to show the effect of that drug The patient has been helped a good deal She has also been getting folic acid by mouth during the past few weeks In the *British Journal of Dermatology* there have been reported cases of tropical sprue cured with folic acid

Dr Maurice Sullivan, Baltimore I should like to suggest to Dr Andrews, in case the eruption does not respond to iodine, the use of sodium caprylate, which has been reported to cure moniliasis when other fungicides fail

DR JOSEPH GOODMAN, Framingham, Mass In cases of ragweed dermatitis, which lasts around the year, it must be remembered that there is often a cross sensitization between ragweed and Pyrethrum I note that other tests were done in this case, but I see no reference to Pyrethrum It would be possible for the patient to be exposed to Pyrethrum the year round That should be considered as a possibility

DR BERNARD APPEL, Lynn, Mass I should like to confirm the observations made by the last speaker and also to point out the fact that many patients subject to ragweed dermatitis are those who live in the country and work around barns where sprays against flies and insects are used, and of course we know that they contain Pyrethrum and products of that family In my opinion it is important to do patch testing with these substances, as well as with the solvents used in insecticides

DR DONALD S MITCHELL, Montreal This man has never been hospitalized I wonder whether it would help to admit him and remove ordinary contacts such as clothing and soaps

DR JACK WOLF The eruption on the torso as seen today is incidental, it developed after a recent cold and may be the result of medication which he received It has no relation to the other eruption This man has been tested with other oleoresins as well as ragweed fractions We have had a number of cases of ragweed dermatitis in which persistent eruptions developed and remained throughout the entire year after several seasonal attacks This persistence may be due to the development of sensitization to other allergens which act at the same site

Lymphoblastoma Mycosis Fungoides with Eczematous Lichenoid and Granulomatous Lesions Presented by DR A BENSON CANNON

OTHER CASES PRESENTED

A Case for Diagnosis (Dermatitis Medicamentosa? Senear-Usher Pemphigus? Dermatitis Herpetiformis?) Presented by DR JACK WOLF

Purpura Hemorrhagica Presented by DR EUGENE F TRAUB

Tuberculosis Cutis Colliquativa Improved by Calciferol Therapy Presented by DR NATHAN SOBEL

A Case for Diagnosis (Macular Atrophy? Lichen Planus Atrophicus?). Presented by DR JACK WOLF

Parapsoriasis Guttata Presented by DR MAX SCHEER

A Case for Diagnosis (Lymphoblastoma? Mycosis Fungoides?). Presented by DR FRED WISE

Dyskeratosis Congenita with Pigmentation, Dystrophia Unguium and Leukoplakia Oris. Presented by DR FRED WISE

Circinate Sarcoid Presented by DR EUGENE F TRAUB

A Case for Diagnosis (Erythroderma Ichthyosiforme Congenitum? Erythroderma Exfoliative Universalis Tuberculosa?) Presented by DR A BENSON CANNON

DR J GARDNER HOPKINS I would question Dr Peck's comments regarding Candida albicans on normal skin, because some years ago Dr Rhoda Benham made careful surveys of normal skin and found other species of Candida but could not find C albicans I think if the differentiation is properly made, one may say that M albicans is rare or nonexistent on normal skin It is found in the normal intestine *I should like to testify to the improvement of this patient under Dr Andrews' treatment* We had her under our care for some time, using sodium caprylate among other things, and she was much worse than she is today

DR DUDLEY C SMITH, Charlottesville, Va In Washington a symposium on antibiotics was held recently There were reports on two substances with fungicidal properties both on local application and on internal injection One was obtained from Bacillus subtilis, although it is not the same as subtilin, and is called "eumycin" The other was developed in the Department of Agriculture last year in an attempt to find something to counteract "tomato wilt" They obtained an extract from tomato leaves which is called "tomatin" Both agents, so the reports stated, have a good therapeutic effect in vitro in various types of fungus infections—monilia, trichophyton and yeast

DR C GUY LANE, Boston It seems to me that the disease moniliasis is increasing We seem to have had more patients in our clinic recently, and I am just as much impressed with the obstinacy of the disease as I was years ago I do not believe we have made much headway in therapy We have had 3 or 4 cases lately in which there was opportunity to make fairly careful studies, and we have run the gamut of therapy We have been interested in trying the method developed at Duke University, where a person with pulmonary moniliasis recovered after serum therapy (J A M A **130** 205 [Jan 26] 1946) I wonder if anything further has been done, perhaps in the way of increasing the titer of rabbit serum by gradually increasing doses A great deal more intensive study is needed in these cases because they are potentially serious Lesions involving the mouth and larynx are obstinate and become generalized, with a fatal ending

DR JASPER L CALLAWAY, Durham, N C We also have our troubles treating moniliasis of the skin at Duke Hospital The patient whom Dr Lane mentioned had pulmonary moniliasis and was treated with a stepped-up course of antiserum and eventually recovered We have not been able to cure any patients with generalized moniliasis of the skin, regardless of the type of treatment

Sarcoidosis (Leprosy?) Presented by DR MAURICE J COSTELLO

A Case for Diagnosis (Periarteritis Nodosa? Eosinophilic Granuloma?) Presented by DR FRANK C COMBES

This case was previously presented before the Section of Dermatology and Syphilology of the New York Academy of Medicine on Jan 7, 1947

Actinomycosis Presented by DR FRANK C COMBES

M A, a girl aged 17, is presented from Bellevue Hospital with a lesion of the left side of the mandible She was previously presented by Dr Maurice J

BROOKLYN DERMATOLOGICAL SOCIETY

Abraham Walzer, M D, *President*
Seymour H Silvers, M D, *Secretary*
March 17, 1947

Mycosis Fungoides in a Patient with Psoriasis Presented by Dr L M Waterhouse

J J, a man aged 46, born in the United States, first consulted me twelve years ago, at which time a diagnosis of psoriasis was made Six or seven years ago he was treated at a well known New York dermatologic clinic where the diagnosis was confirmed clinically and histologically He had received ultraviolet rays, coal tar preparations and other topical medication There was no history of his ever having received arsenic preparations Two years ago the lesions became raised and tumor like At that time a biopsy specimen from one of these lesions was reported as suggesting lymphoblastoma, but no more definite diagnosis was made The biopsy was repeated two months ago by another histopathologist, who suggested the possible diagnosis of mycosis fungoides

Results of repeated serologic tests for syphilis were negative Results of blood cell counts and urinalyses were normal

Examination shows a generalized eruption There are quarter-sized to dollar-sized flat, red, scaly patches There are a few lesions on the lower part of the back and thighs, which are raised and tumor like The face shows an ill defined erythema with scaling On the scalp are similar patches with alopecia

DISCUSSION

Dr Seymour H Silvers This is a most unusual case It seems that the diagnosis of psoriasis was established independently by different competent dermatologists This diagnosis was corroborated by histologic studies At present there are seen a sufficient number of lesions which are infiltrated and tumor-like to warrant a clinical diagnosis of granuloma fungoides However, we cannot completely ignore the findings of two able histopathologists who failed to corroborate the diagnosis of granuloma fungoides It is not unusual for the histopathologist to fail the clinician when the latter needs him most

Dr L M Fruchtbaum The picture is not that of psoriasis On the other hand, there are two large lesions and numerous smaller ones on the body and extremities which are definitely infiltrated In spite of the fact that the patient feels and looks physically well, I believe that this is a case of mycosis fungoides

Dr E A Gauvain I believe that the disease in this case was originally mycosis fungoides, as it is now I did not see any lesions typical of psoriasis on this patient, although such a diagnosis might have been considered in a few lesions had they been the only ones present I have never seen a case of undisputed psoriasis, even though followed through many recurrences, that terminated as mycosis fungoides Clinically there is now a polymorphous type of lesion, changing in character, of a dusky color, causing some itching and finally developing into nodules, which, to my mind, are typically mycosis fungoides

Dr Abraham Walzer Clinically, this is a case of mycosis fungoides The disease developed in a manner that it does in many cases It never was psoriasis, irrespective of the fact that histologically it was first reported as psoriasis

Costello at the New York Dermatological Society in January 1947 and by Dr Emanuel Muskatblit at the Section of Dermatology and Syphilology of the New York Academy of Medicine on Feb 4, 1947

DISCUSSION

DR. GEORGE M LEWIS At a recent meeting in Cleveland, Lamb, of Oklahoma City, discussed the therapy of actinomycosis and stated that it should include (1)

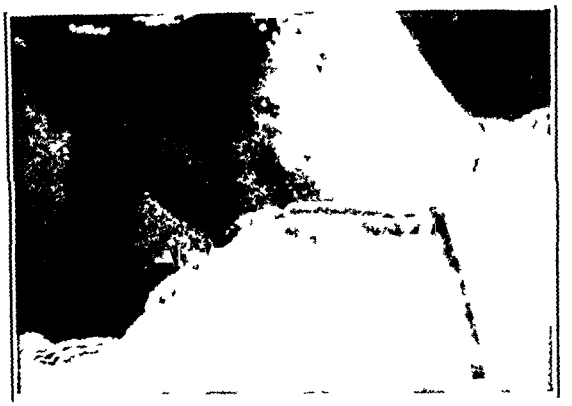


Fig 2—Periarteritis nodosa in a woman aged 35

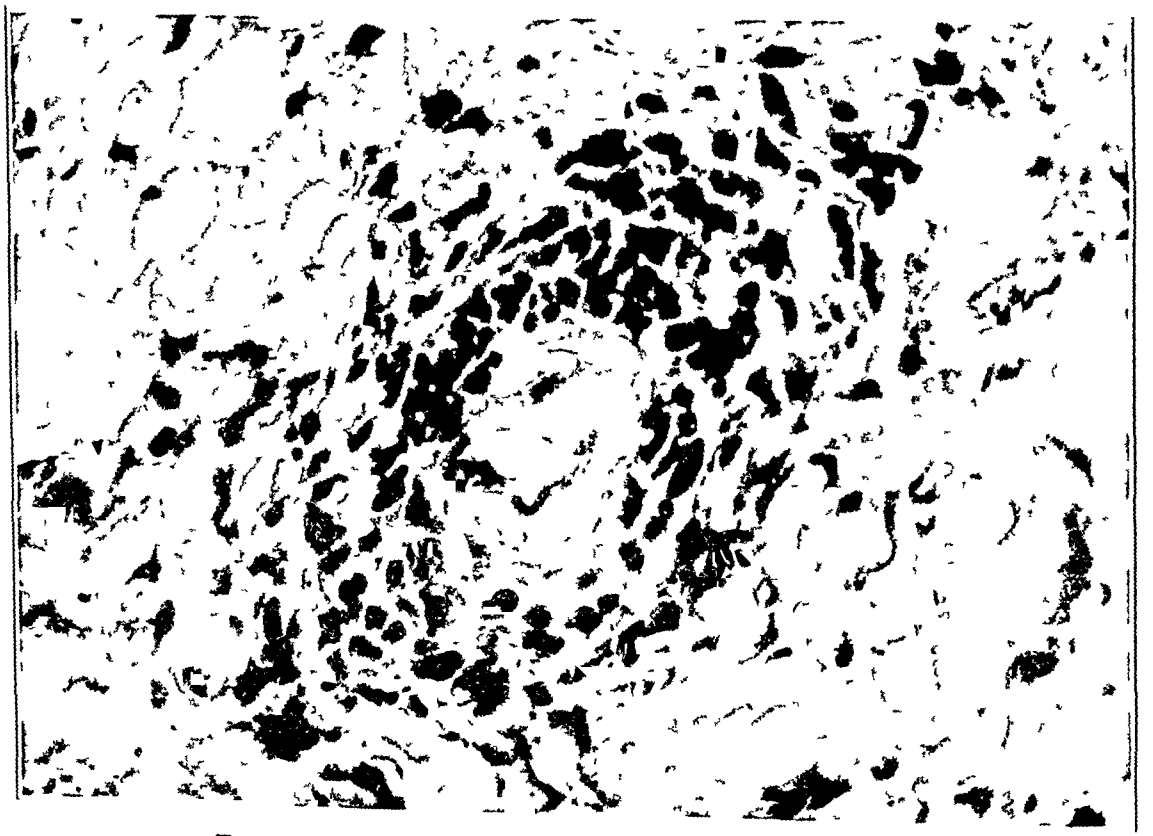


Fig 3—Photomicrograph of area of periarteritis nodosa

penicillin in large doses, which this patient has received, (2) one of the sulfonamide drugs, and (3) roentgen irradiation He favored this combination of remedies as superior to any one alone or to any other type of treatment now available

Mycosis fungoides may begin with what may appear to be psoriasis, parapsoriasis, eczema or any other condition I believe that just as the clinical picture, at the start, may be atypical, so the histologic picture may be more or less vague and indefinite At the present, this man shows lesions which, to my mind, are classic examples of mycosis fungoides

Epithelioma of Penis Presented by DR S I GREENBERG

Multiple Keloids Presented by DR MAX LERNER

J G, a girl aged 12, was seen at the Kings County Hospital Dermatologic Clinic on March 3, 1947 She had chickenpox in October 1946, and "marks" developed where there had been blisters

There are hard nodules, pea to bean size, distributed on the face, neck, abdomen and thighs Some are colorless and others yellowish white A few are erythematous with telangiectasia All the lesions are limited to the sites of the original varicella blisters There is no history of keloidal scars from previous injuries

DISCUSSION

DR ABRAHAM WALZER The keloid tendency does not have to be present during the entire life of the patient There may be periods when the tendency does not show itself My experience has been that if keloid is treated before it has been present six months, with roentgen rays, there is a chance of flattening of the lesion After six months, roentgen therapy is of no value This has been explained on the principle that connective tissue cells mature in about six months When the cell becomes fully mature, it cannot be reduced, but as it is growing and developing (that is, up to six months), its growth can be stopped No matter how much roentgen therapy is given after six months, it is of no value However, if the lesion is excised and roentgen rays given, the lesion may be suppressed

Generalized Sarcoidosis Presented by DR MAX LERNER and DR FRANK D JENNINGS JR (by invitation)

Abraham Walzer, M D, *President*

Seymour H Silvers, M D, *Secretary*

April 21, 1947

Xanthoma Tuberosum Presented by DR C T CHIARAMONTE

Xanthomatosis Juvenilis Presented by DR C T CHIARAMONTE

V S, a white girl, aged 5 years, has several discrete, bean-sized, yellowish nodules on the face and neck Her liver is enlarged to 2 fingerbreadths below the costal margin with an even, smooth edge

This child was first seen when she was 6 weeks old She showed many shiny, yellowish nodules which were generalized and of varying sizes There was a reddish halo around the lesions Some of the larger ones were oval in shape Many of the lesions showed multiple punctate depressions at the follicular orifices Lesions were also found on the mucous membranes of the mouth The lesions were noticed soon after birth

Dermatitis Factitia Actinomycosis? Presented by DR THOMAS N GRAHAM

Pachyonychia Congenita (Keratosis Palmaris et Plantaris Dystrophia Unguium and Leukoplakia Oris) Presented by DR FRED WISE

S H, a woman aged 40, and L H, her son aged 16, were previously presented before the Manhattan Dermatologic Society on January 14 by Dr Fred Wise

Both patients show hard, thick, painful, hyperkeratotic, lemon-colored growths on the soles, heels and toes The toe nails and finger nails are elongated, curved, discolored and dyskeratotic There are leukoplakic patches on the buccal mucosa



Fig 4—Dermatitis factitia in a woman of 38

and also on the tongue in the mother, who in addition presents dry, scaly, diffuse, seborrheic patches on the scalp Her basal metabolic rate was —20 per cent in February, and the son's was —14 per cent

DISCUSSION

DR FRED WISE This is the second case of the kind to be described in this country Cole and his collaborators described a case fully in the ARCHIVES, and this case is almost an exact replica of theirs The problem is one of therapy Both patients are practically crippled One lesion on the mother's knee was excised and a full thickness graft applied, and the growth recurred promptly in the area of the graft Dr Peck suggested administration of large doses of vitamin A, and this is being given, but too little time has passed to expect results I am pessimistic about any treatment whatever, except possibly an orthopedic procedure to permit the patient to walk with some degree of comfort

The infant was placed on a low fat diet and was reexamined a year later It was observed that occasionally there was a generalized flushing of the skin During the period of observation, some of the lesions appeared vesicular, the mouth lesions disappeared and the cutaneous nodules grew in size Many of the lesions showed flattening at the periphery, and a few lesions disappeared Since then all lesions have undergone involution except those on the face and neck The skin at the sites of former lesions has become brownish red There has at no time been any jaundice or pigmentary changes affecting the normal skin

A biopsy performed during infancy revealed a dense infiltrate in the cutis, consisting of epithelioid cells, the cytoplasm of which had a vacuolated appearance and simulated fat cells

DISCUSSION

DR SEYMOUR H SILVERS I followed 2 cases of xanthomatosis juvenilis for many years The patients came under my care during the first month of their lives I watched new lesions appear, and, as the children became older, the lesions gradually flattened out and finally disappeared I believe that, regardless of therapy, the lesions of xanthoma juvenilis will disappear when the child reaches the age of 6 to 7 years It is likely that xanthomatosis juvenilis should be classified with the nevi rather than with the diseases due to metabolic disturbances

DR ABRAHAM WALZER These patients should have a complete determination of the lipids of the blood Increased cholesterol does not necessarily imply that every case of xanthomatosis is due to cholesterol disturbance If any other fats are disturbed, the cholesterol may be increased in the blood To what is the yellowness of the cholesterol lesions due? Cholesterol and its esters are white, but the lesions are not The yellowness is probably due to a lipofuscin substance found in the fat

Tuberculosis Cutis with Papulonecrotic Sarcoid-Like and Colliquative Lesions Presented by DR S B FRISCHBERG

Alopecia Congenita Presented by DR C T CHIARAMONTE

D B, a white girl aged 9 years, has scant growth of hair on the scalp and eyebrows The deficiency is more evident in the frontal region There is pronounced follicular keratosis on the nape of the neck The child weighed 6 pounds, 2 ounces (2,778 Gm) at birth, was a breech presentation at delivery and gained weight more slowly than the average infant Since birth the hair on the scalp had always been sparse

The laboratory examination revealed absence of arsenic in the urine, a basal metabolism of + 13 per cent and a normal reaction for specific dynamic action of proteins A roentgengram of the sella turcica was normal

DISCUSSION

DR SEYMOUR H SILVERS Often, in addition to absence of or sparse hair, other ectodermal defects are seen It is not unusual to observe alopecia with dental and ophthalmic defects This child is mentally alert and bright.

DR JOEL SCHWEIG I am in favor of the diagnosis of the presenter, but I would advise cultures be made from the scalp and hair as the picture may turn out to be one of favus



Fig 5—Hyperkeratotic growths of pachyonychia congenita in a boy aged 16



Fig 6—Dyskeratotic toe nails and finger nails in same boy as in figure 5

Epidermolysis Bullosa Congenita Presented by DR C T CHIARAMONTE

G O, a white boy aged 4 years, has numerous bullae on the dorsum of the feet, some of which are hemorrhagic The toe nails and finger nails show atrophic and dystrophic changes Healed, erythematous lesions may be seen on the elbows and knees

There is no consanguinity of the parents It is interesting to note that this child has a nonidentical twin brother who is normal This child was first observed a few days after birth At that time, there were numerous cloudy bullous lesions scattered on the body, which I diagnosed as pemphigus neonatorum Culture from the bullae revealed the presence of Staphylococcus albus The lesions disappeared after treatment with sulfonamide drugs locally and internally Since then, however, blisters have been noticed by the parents to be reappearing on the extensor surfaces of the elbows and knees, on the dorsa of the feet and in the mouth

A Case for Diagnosis (Hodgkin's Disease?) Presented by DR C T CHIARAMONTE

L A, a white man aged 43 years, has a generalized, itchy eruption consisting of isolated, large, serrated papules These papules are brownish red, and some of them are excoriated There are also irregular groups of large vesicles, the tops of many present a small yellowish crust located on the extensor surfaces of both legs, arms and forearms and on the dorsa of the hands On the thighs the lesions have spread peripherally and form patches of crusted vesicles Groups of vesicles are present on the face, chest and abdomen Several of the original lesions have left a brownish pigmentation

The patient has had papular lesions and itching for the past seven months He first presented himself for treatment in January 1947, after having been treated elsewhere for scabies The past history reveals that the patient has had pulmonary tuberculosis, which was recognized in 1928 and was pronounced arrested in 1935, after a phrenicectomy In 1943 he received treatment for spastic colitis

A recent roentgenogram of the chest and examination of the gastric contents for tubercle bacilli did not reveal any abnormalities A biopsy of one of the papules performed in March revealed moderate acanthosis and parakeratosis with some hyperkeratosis The epidermis was infiltrated with eosinophils The corium contained many eosinophils, round cells and proliferating fibroblasts This inflammatory infiltrate was grouped around the small blood vessels The results of the urinalysis and hemogram were within normal limits The cholesterol content of the blood was 197 8 mg per hundred cubic centimeters and the cholesterol esters were 67 9 mg Roentgenograms of the long bones showed no abnormalities

DISCUSSION

DR C T CHIARAMONTE The biopsy was performed on one of the nodular purplish brown, persistent lesions I have known of cases of early Hodgkin's disease which was mistaken for scabies The patchy eruption on the arms, forearms and legs has appeared only in the past two months I shall observe him closely In the past few months, there has been a rise in the white blood cell count

DR NATHAN PENSKY The suggestion of Dr Chiaramonte must be seriously considered Several articles in the current literature have appeared on eosinophilic granuloma However, I have seen a number of patients who have been overtreated for scabies in which an eczematized eruption developed which clinically resembled

Incontinentia Pigmenti Presented by DR J GARDNER HOPKINS

J A M, a girl aged 5½ months from the Vanderbilt Clinic, was previously presented by Dr Helen O Curth before the Section of Dermatology and Syphilology of the New York Academy of Medicine on March 4, 1947

Most noticeable on the inner aspect of the thighs but visible also on the sides of the trunk are wavy parallel bands of hyperpigmentation in typical zebra pattern The skin is otherwise normal

DISCUSSION

DR FRED WEIDMAN, Philadelphia A number of years ago I performed an autopsy on an infant with peculiar transverse bands of pigment across the abdomen, but in paraffin sections I could not find the pigment which was to be expected Perhaps Dr Hopkins has had the same experience, because in his sections the pigment was inconspicuous However, in frozen sections, it was conspicuous indeed It is true that melanin pigment is not supposed to be dissolved in our histologic embedding agents, but perhaps in Dr Hopkin's case, too, frozen sections would show the pigment more plainly than do the histologic sections I reported my case under the name of "Transverse Hyperpigmented Lines of the Thorax and Abdomen of a Negro Infant" in the ARCHIVES (**37** 517-523 [Aug] 1919)

DR J GARDNER HOPKINS Was the pigment in the epidermis or in the chromatophores?

DR FRED WEIDMAN, Philadelphia In the epidermis

DR GERALD F MACHACEK This type of disorder has also been reported as familial chromatophore nevus by Naegeli and as melanodermatosis congenita by Siemans

DR J GARDNER HOPKINS I do not believe that this case is parallel to Dr Weidman's It corresponds to the cases described by Naegeli and by Bloch and Sulzberger in which pigment was in the chromatophores under the skin and not in the epidermis

A Case for Diagnosis (Behcet's Syndrome? Pemphigus? Leukemia Cutis?) Presented by DR EUGENE F TRAUB

A Case for Diagnosis (Lichen Planus and/or Lupus Erythematosus of Lips and Tongue Oriental Sore of Forearm) Presented by DR MAURICE J COSTELLO

G R, presented from Bellevue Hospital, was born in the United States and was taken to Greece when he was 14 years old, where he remained until about four months ago He was a guerilla fighter during the past two years in Greece. He does not smoke

About 15 months ago an erythematous patch appeared on the patient's right forearm, persisting until about three months ago, when it developed into an ulcer After biopsy was performed at this site the ulcer healed spontaneously A hyperpigmented scar can be seen

About four months ago a small superficial red area appeared on the left side of the dorsum of the tongue It increased in size to that of a 25 cent piece, became superficially eroded with a grayish pellicle-like border, and caused some pain when the patient was eating and drinking

During the past three weeks reticulated whitish streaks on the lower lip suggestive of lichen planus have developed A small superficial erosion has recently developed on the center of the tongue, medial to the one just described There has been no regional adenopathy

the rash in the case presented tonight The histologic observations in the present case would lead one to suspect the possibility of a lymphoblastoma

DR C T CHIARAMONTE Another thing of interest is the tuberculous background I feel that Hodgkin's disease and tuberculosis are in some way related

DR JOEL SCHWEIG I have the feeling that the diagnosis of Duhring's disease is the right one, as I have seen several instances of that condition which resemble clinically the case presented tonight My suggestion is that the patients be tested with potassium iodide, internally and externally, and that he be treated with sulfapyridine

Mycosis Fungoides, Developing On Parapsoriasis(?) Presented by DR C T CHIARAMONTE

Abraham Walzer, M D, *President*
Seymour H Silvers, M D, *Secretary*
May 19, 1947

Generalized Scleroderma Presented by DR L M FRUCHTBAUM

A M, a woman aged 70, was admitted to the Unity Hospital on Jan 6, 1947, because of acute cardiac decompensation Examination revealed edema of the lungs and of the legs The patient gave a history of progressive dysphasia for the previous three years, during which time she had noticed thickening and hardening of the skin of the forehead and face with inability to open the mouth wide The patient also noticed that she was unable to smile or frown and experienced difficulty in swallowing foods, particularly hard foods The hardening of the skin extended to the neck, shoulders, chest, back and thighs Examination revealed a waxy smooth skin adherent to the underlying soft tissues on the face, neck, trunk, shoulders and thighs The fingers and toes were not affected

The hemogram was within normal limits except for a leukocyte count of 12,500 per cubic centimeter Blood chemistry studies gave normal values for sugar and cholesterol, but the urea nitrogen was elevated to 28 5 mg per hundred cubic centimeters, and creatinine to 2 mg per hundred cubic centimeters The basal metabolic rate was —36 per cent The urine was normal Histologic examination of a specimen of skin showed scleroderma

DISCUSSION

DR JOEL SCHWEIG In view of the fact that there is so much edema present on the neck, as well as the lower extremities, I feel that the process is a deep-seated one and may be scleredema of the infectious type as described by Buschke Should it be of infectious origin, treatment with penicillin or sulfonamide drugs would be indicated and the prognosis would be more favorable A biopsy should aid in the final diagnosis

DR JACOB SKEER I also believe that there is too much edema present and that the extension of the lesion was rather rapid By this time there should be contracture of the tissues and other signs, like pigmentation The edema is of the nonpitting type and suggests Buschke's disease I think that a biopsy would give more information

DR SAMUEL I GREENBERG I think that this is scleroderma Scleredema is described in young adults, it follows infectious disease and is transient These aspects are not present in this case

Necrobiosis Lipoidica Diabeticorum, Lesions on the Legs Presented by DR S ROTHMAN and (by invitation) DR Z FELSHER and DR L RUBIN

Linear Scleroderma Presented by DR S ROTHMAN and (by invitation) DR H KRYSA

Nevus Unius Lateris with Chronic Inflammation? Presented by DR S ROTHMAN and (by invitation) DR E L LADEN

Marcus R Caro, M D, *President*

Leonard F Weber, M D, *Secretary*

March 19, 1947

Lichen Sclerosus et Atrophicus and Rosacea with Acne and Rhinophyma in a 49 Year Old Woman Presented by DR D OMENS and (by invitation) DR H OMENS and DR J GRAFFIN

Lichen Simplex Chronicus of the Vulva of Three Years' Duration in a Seven Year Old White Girl Presented by DR DAVID V OMENS and (by invitation) DR H OMENS and DR N L BAKER

Mycosis Fungoides d'Emblée Presented by DR D OMENS and (by invitation) DR H OMENS and DR N L BAKER

A Case for Diagnosis, Postinflammatory Cystic or Keloidal Lesions of the Hands Presented by DR H RATTNER and (by invitation) DR J GRAFFIN

A Case for Diagnosis (Actinomycosis? Ecthyma?) Presented by DR M H EBERT and (by invitation) DR J GRAFFIN

Widespread Cutaneous Nodular Sarcoidosis with No Systemic Manifestations Presented by DR H RATTNER and (by invitation) DR RODIN and DR J GRAFFIN

Classic Acrodermatitis Chronica Atrophicans with Involvement of the Palms, Atrophy, Pseudosclerodermatous Plaques and Fibromas Presented by DR M EBERT and (by invitation) DR V LEAF and DR J GRAFFIN

Generalized Argyria from the Ingestion of Argyrol, One Ounce a Week for Five Years, to Prevent "Colds" Presented by DR M EBERT and (by invitation) DR J GRAFFIN

Bizarre Pigmentation, Cause Undetermined in a Pituitary Type Dwarf Presented by DR T CORNBLEET and (by invitation) DR D COHEN and DR N L BAKER

Kaposi's Varicelliform Eruption in an Infant Presented by DR D V OMENS, DR S J ZAKON and (by invitation) DR H OMENS and DR N L BAKER

G V, a 4 months' old white boy, had eczema of the face since the age of 1 week Five day ago vesicles appeared on the cheeks Physical examination disclosed a mildly toxic infant The temperature ranged from 100 to 102 F rectally Groups of umbilicated vesicles situated on an erythematous base are present on the cheeks, chin and eyelids There is a cluster of pinhead-sized vesicles on the tip of the tongue

The Mantoux reaction was negative, erythrocytes were 5,230,000 and leukocytes 5,150, with 30 per cent polymorphonuclear cells, 63 per cent lymphocytes, 1 per cent eosinophils and 7 per cent monocytes

On March 18, 1947, a rabbit's eye was scarified and inoculated with blister fluid from one of the lesions

DISCUSSION

DR M H EBERT I believe that this is an instance of Kaposi's varicelliform eruption The herpetiform vesicles in this condition are of short duration because they are quickly erupted The vesicles in the mouth occur in groups as they do in ordinary herpes Ordinarily this eruption is associated with a considerable rise in temperature and with more toxemia than is present in this patient Penicillin has been administered and found to be of value in reducing the toxemia Dr Baker inoculated the cornea of a rabbit with material from one of the lesions Results were negative At the present moment there is no proof that this is due to infection with the herpes simplex virus Had the inoculation been positive at the end of twenty-four hours, there would be extensive involvement of the cornea of the rabbit with inflammatory exudate If the cornea is then removed and fixed with Zenker's solution or mercuric chloride in alcohol, the sections will show nuclear inclusions in the epithelial layers at the site of the scratch marks identical with the inclusions that are present in the early lesions of ordinary simplex

DR FRANCIS W LYNCH, St Paul In such a case one may reasonably question whether the eruption is the result of virus infection or pyogenic infection or both Umbilication of vesicles is seen in some superficial pyodermas and apparently a few such cases have been reported as of Kaposi's varicelliform eruption In one instance an epidemic of such cases was reported In recent years a number of workers have demonstrated the herpetic virus in patients with Kaposi's disease, but none claim it to be the only cause, pyogenic infection could become superimposed

In this case of Dr Omens and Dr Baker, the grouping of the lesions in the submaxillary area and the eruption on the tongue make me think that the condition is herpetic It is odd that the patient is not more ill, as the first herpetic infection, even when localized, usually produces considerable febrile reaction It may be possible to find the source of the infection by questioning or examination of the persons who had recently handled the child In such a young child the source should be exogenous rather than endogenous

DR S J ZAKON I saw this baby four days ago, and his temperature was 105 F rectally The child was then much more toxic When I saw him two days later, after two days of penicillin therapy, he had improved very much

DR J E GINSBERG I would like to ask Dr Lynch about the prognosis Would you hesitate to hospitalize such a patient without isolation?

DR FRANCIS LYNCH I would not hospitalize such a patient without isolation I think that herpes simplex should be regarded as an infectious disease, and on a

DR DAVID M DAVIDSON I think that this is scleroderma The patient also has cardiac disease, and the pitting of the legs has nothing to do with her scleroderma I do not believe that this is scleredema of Buschke because the duration of the condition is three years and there is no history of a preceding infection

Urticaria Pigmentosa Presented by DR L M FRUCHTBAUM

DISCUSSION

DR C B LOCASTO It has been found that in animals given a diet free of vitamin A large numbers of mast cells develop in the tissues of the body In view of this, it is suggested that the patient receive large doses of vitamin A

Case for Diagnosis (Granuloma Annulare?). Presented by DR L M FRUCHTBAUM

Case for Diagnosis (Necrobiosis Lipoidica Diabeticorum? Granuloma Annulare?) Presented by DR I N HOLTZMAN

The patient, a white housewife aged 51, was first seen in the outpatient department of the Jewish Hospital of Brooklyn on May 12, 1947, with the following history

About five weeks prior to admission, she first noticed a nonitching eruption on both forearms and eyelids, which followed a mild abrasion of the left forearm The eruption has remained unchanged since its onset Her past history revealed the existence of diabetes mellitus of at least ten years' duration and a mild hemostatic eczema of the right ankle of about seven years' duration

Examination on admission revealed a papular eruption on the volar aspect of both forearms and eyelids The lesions varied in size from that of a pinhead to that of a pea and were faintly erythematous, and the larger papules were slightly yellow There was no characteristic grouping or configuration of any of the lesions

A biopsy of a lesion of the left forearm showed degeneration, necrobiosis and homogenization of the collagen with nuclear debris Surrounding and infiltrating into this zone were large collections of epithelioid foam cells Small round cells were occasionally seen Blood chemistry studies revealed a concentration of sugar of 181 mg and cholesterol of 261 mg per hundred cubic centimeters

DISCUSSION

DR JOEL SCHWEIG In my opinion the clinical features of the case fit in well with the diagnosis of lichen ruber moniliformis, which was well reviewed by Wise and Rein in 1936 The shape of the lesions, the color and the distribution are typical Although there is only one area on the right wrist presenting the moniliform features, it should be considered lichen ruber moniliformis, as those features may appear later in abundance The histologic observations are also like the microscopic features of lichen ruber moniliformis

DR DAVID M DAVIDSON When the patient was first seen at the clinic, a few diagnoses were mentioned, among them lichen moniliformis and lichenoid sarcoid When I examined the slide and saw that the main histologic changes

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consisted of local granular necrosis with cellular debris surrounded by many epithelioid cells and a few connective tissue cells, I was inclined to consider the case as one of granuloma annulare, although the patient did not have any ring lesions I have seen a few patients with granuloma annulare with scattered papules, but they also had the typical annular lesions However, Hartzell (*J A M A* **63** 230 [July 18] 1914) and Stilhans (*J Cutan Dis* **37** 580, 1919) each reported a case of granuloma annulare without ring lesions, and the latter mentioned many others who had observed similar cases

The patient has definite lichenoid papules, some resembling lichen planus, although the lesions are softer to the touch than those in lichen planus There is no moniliform arrangement and no waxy papules as were described in lichen moniliformis Another interesting point in this case is that the patient has diabetes but clinically the lesions do not suggest necrobiosis lipoidica diabeticorum, and histologically one often finds extensive vascular damage in necrobiosis as well as in lichen moniliformis, features not found in this case and usually not seen in granuloma annulare In consideration of all this, I am inclined to consider this as a case of granuloma annulare

Xanthoma Tuberosum Presented by Dr L M Fruchtbaum

Epithelioma of the Cheek in a Woman Aged Twenty Years Presented by Dr Seymour H Silvers

Acrokeratosis Verruciformis of Hopf Presented by Dr C B Locasto

M C, a Negro woman aged 52, stated that she has had thick skin on the palms and soles and wartlike growths on the back of her hands since birth There are no subjective symptoms The palmar and plantar surfaces are hyperkeratotic The dorsal aspects of the hands and feet and the distal parts of the forearms are studded with numerous, discrete, confluent and flat-topped verrucalike polygonal papules The nails are frayed distally, have vertical linear striations and are brittle

DISCUSSION

Dr Joel Schweig This is an unusual case and of a type rarely seen at our meetings I agree with the diagnosis Acrokeratosis verruciformis and epidermodysplasia verruciformis are different in that the latter appears in persons with consanguineous parents and is associated with malignant degeneration of the lesions The concept of this condition is that it is of nevoid character

Tinea Capitis in an Adult (Microsporon Lanosum) Presented by Dr E A Gauvain

T A, a widow aged 73, had been losing hair for four months She complained of slight itching of the scalp She had no recollection of direct contact with dogs or cats, but a dog had been a recent visitor to one of her neighbors

The hair of the scalp is thick and long, with many areas showing slight erythema and definite defluvium without any sharply defined areas of alopecia Under the Wood light, fluorescent hairs mingled with nonfluorescent hairs are seen throughout the scalp A culture of infected hair grew Microsporon lanosum

dermatologic service the patient should be isolated I am sure that I have seen the infection carried by and transferred by attendants

Tuberculosis Colliquativa of the Sternum in an Eleven Year Old Negro Girl Presented by DR D V OMENS and (by invitation) DR H OMENS and DR B YAFFEE

Generalized Acne Scrofulosorum, Ecthyma Presented by DR F E SENEAR and STAFF

R S, a 4 year old Negro boy, was admitted to the Illinois Research and Educational Hospitals for the treatment of tuberculosis of the right hip For six months a generalized eruption had been present and large ulcerations had appeared on both legs

Examination revealed numerous folliculopapular lesions distributed over the entire cutaneous surface but most concentrated on the extensor surfaces of the extremities A few lesions exhibited central necrosis, older lesions were represented by slightly depressed scars, depigmented at the centers and with hyperpigmented borders A fading eruption of tiny lichenoid papules was present on the sides of the trunk Large granulating ulcers were noted over the anterior aspects of both legs

A bullous reaction developed after skin testing with 1 10,000 old tuberculin The report of biopsy is not yet available

DISCUSSION

DR H E MICHELSON, Minneapolis It has never been clear to me why certain types of tuberculosis respond to roentgen therapy and others do not For example, bone and most skin lesions do not respond while glandular tuberculosis and certain peritoneal types do There are many other facts about glandular tuberculosis that are most interesting, especially the seasonal incidence One does not see many patients with generalized tuberculous eruptions Recently Schmidt wrote a good article on these eruptions in the German dermatology journal (*Archiv für Dermatologie und Syphilis*)

Dermatitis in Red Area of Tattoo, Reaction Positive to Patch Test with Ammoniated Mercury, Negative with Cinnabar Presented by (by invitation) DR EVERETT T DUNCAN and DR CLARK F JOHNSON

Psoriasis Verrucosa, Arthropathy and Koebner's Phenomenon Presented by DR S ROTHMAN and (by invitation) DR J MCCREARY

DISCUSSION

DR MARY S SHERMAN It is variously estimated that 2 to 4 per cent of patients with symptoms of chronic arthritis have psoriasis Conversely up to 12 per cent of patients with psoriasis may be expected to have joint symptoms at one time or another Since the joints are rarely involved severely enough so that operation is indicated, reports of the pathologic changes are few

The clinical characteristics of so-called psoriatic arthritis are well known Males are affected more than females Although any joint or combination of joints may be involved, the joints most commonly and characteristically troublesome are the terminal interphalangeal joints of fingers and toes, and there are usually associated typical nail changes It is especially noteworthy that the joint

CHICAGO DERMATOLOGICAL SOCIETY

Francis W Lynch, M D, *President*

Leonard F Weber, M D, *Secretary*

Feb 19, 1947

Pemphigus Vulgaris Presented by DR M H EBERT and (by invitation) DR N L BAKER

A Case for Diagnosis (Erythema Perstans?). Presented by DR T CORNBLEET and (by invitation) DR D COHEN and DR J GRAFFIN

Lupus Pernio? Presented by DR S ROTHMAN and (by invitation) DR Z FELSHER and DR L RUBIN

Sarcoidosis, Keloidal Nodules on the Nose of a Young Negro Woman Presented by DR H RATTNER and (by invitation) DR H RODIN and DR J GRAFFIN

A Case for Diagnosis (Lupus Erythematosus in a Girl of 17 Years). Presented by DR D OMENS, DR S J ZAKON and (by invitation) DR H OMENS and DR J GRAFFIN

Systemic Blastomycosis Presented by DR D OMENS and (by invitation) DR H OMENS and DR J GRAFFIN

S W, a Negro woman aged 39, on Dec 24, 1946 precipitously delivered a full term baby while on the street Several days later she noticed a few nodules on the right forearm, which gradually grew to form abscesses In the next two months numerous fluctuant, hen's-egg-sized abscesses appeared on the face and extremities, and, in addition, warty lesions developed on the face and trunk For the past few weeks she has had fever, "night sweats," headache and malaise, but no symptoms referable to her gastrointestinal, respiratory or genitourinary tract Until the time she entered the Cook County Hospital, she had nursed her apparently healthy baby Her other four children and her husband have been in good health She has not been out of Chicago in the past two years and has no contact with flowers, gardening or animals

Examination reveals numerous fluctuant, tender, subcutaneous abscesses scattered on the face, extremities and back, varying from 1 to 5 cm in diameter In addition, there are verrucous nodules on the face and trunk Physical examination revealed no other abnormalities While in the hospital she has had a low grade fever daily, accompanied with headache and malaise

The Kahn reaction of the blood was negative The urine was normal The blood examination showed erythrocytes 4,600,000, hemoglobin 67 per cent and leukocytes 22,200 Sterile aspiration of a subcutaneous abscess resulted in recovery of blastomycetes on culture Direct sodium hydroxide preparation revealed numerous round doubly refractile bodies, some of which were budding The blastomycin intracutaneous test revealed a 12 mm erythematous papule at 24 hours, but at 48 hours the papule was only 5 mm in diameter The roentgenogram of the chest revealed a normal cardiothoracic ratio There was a small discrete

manifestations do not respond to treatment directed toward the arthritis, but improve miraculously as the cutaneous lesions subside

As a rule, therefore, the arthritic manifestations subside between exacerbations of the cutaneous lesions and in the intervals there are usually no symptoms of permanent residual damage Occasionally the joints are irritated sufficiently so that they do not return to normal, and there have been reports of complete ankylosis

In the present case arthritic symptoms appeared at the early age of 17, one and a half years after the onset of the cutaneous disease The psoriasis was essentially untreated and grew progressively worse During the next two and a half years, more and more joints became involved, and none of them improved The patient had been completly incapacitated by the pain in his knees

The roentgenograms of this boy's knees show little other than regional atrophy and beginning degenerative changes The cartilage space is well preserved, but there is irregularity of the articulating surface of the patella and small osteophytes forming at its periphery The roentgenograms of the hands show more typical changes In the right hand the terminal two joints of the fifth finger have been largely destroyed and marginal absorption of the ends of the phalanges is evident. In the left hand similar changes are observed in the terminal joint of the long finger and in all the joints of the index finger In the metacarpophalangeal joint there has been peripheral destruction of the articular cortex, so that only the central portion is visible

When biopsy of the right knee joint was undertaken, the cutaneous lesions had begun to show some improvement Exploration of the knee joint revealed gross damage There was severe synovitis which had resulted in dense adhesions The synovial membrane had grown over the joint surfaces, so that the tibia was scarcely visible The patella was encircled by numerous osteophytes and its articular cartilage was completely destroyed except for a few soft gelatinous remnants What was visible of the surfaces of the tibia and femur appeared to be normal This first section is from the synovial membrane It shows the grossly hypertrophied villi The most striking change is the great amount of well organized, vascular, fibrous thickening, with relatively few signs of inflammation, an observation which was noted by Bauer and his associates The blood vessels are also somewhat sclerotic This is in contrast to the chronic inflammatory character of this synovial membrane taken from a patient with Still's rheumatoid arthritis

A piece of bone and cartilage was removed from the edge of the femoral condyle in an area where the articulating surface looked normal, but the section reveals advanced changes No articular cartilage remains It has been entirely replaced by a collagenous type of fibrocartilage which contains numerous blood vessels Beneath the cortex is seen a sort of chronic granulation tissue Between these two the bony cortex has been thinned to a narrow plate, which in one spot is almost disrupted

It is, of course, not possible to say whether these changes are characteristic of psoriasis They are certainly not like those one associates with rheumatoid arthritis In fact, they are not quite like any of the known chronic arthritides It will take further study before we understand how this appearance is produced and what it means

Psoriasis Verrucosa, Developing During Treatment Presented by DR S ROTHMAN and (by invitation) DR L RUBIN

DISCUSSION

DR STEPHEN ROTHMAN The relationship between psoriasis and arthropathia according to Julius Bauer is due to debility of conjugated genes He published

density visualized in the left apical region superimposed on the posterior border of the third left rib, with the suggestion of a drainage band extending to the left hilus

Histologic section revealed acanthosis with edema of the prickle cell layer The corium is edematous and contains a cellular infiltrate composed of lymphocytes, plasma cells and leukocytes Deep in the corium there are numerous double contour bodies with a few giant cells

DISCUSSION

DR. OLIVER S ORMSBY I had been practicing only about a year when I was called to see a patient who was supposed to have tuberculosis A man of middle age had lesions on the face and on the extremities The lesions on the face were fairly typical of blastomycosis, but the lesions on the extremities were very different In those areas there were subcutaneous nodules, abscesses and ulcers, with pus oozing out of the lesions I took a specimen to the office and demonstrated Blastomyces The patient was very ill and died shortly thereafter At autopsy I was able to demonstrate Blastomyces in the lungs, liver, spleen, kidneys and bones That was the first case on record in which there was systemic blastomycosis involving all the tissues

During the next three or four years I saw 4 or 5 more cases, and it was shown that this organism attacks every tissue in the body At autopsy the doctor in charge pricked his finger, and within a little while blastomycosis developed in that finger, and within two or three months he had systemic blastomycosis In our early experience practically 100 per cent of the patients died Since that time a certain percentage recover

DR M J REUTER, Milwaukee One of our residents checked over our records on systemic blastomycosis and was able to find 38 cases of the generalized type Of this number he was able to trace 26 One patient is still alive after ten years and another is alive after two years

Paraffinoma Presented by DR T CORNBLEET and (by invitation) DR D COHEN and DR J GRAFFIN

C H, a white woman aged 63, about twenty-five years ago, had wax injected into both cheeks and the forehead for cosmetic purposes At present she is in a medical ward at the Cook County Hospital with arteriosclerotic heart disease and possible endocrine disturbance Examination revealed a firm mass, 5 cm in diameter, in both cheeks, and a smaller one between the eyebrows The overlying skin is bound down to the masses and is bluish red

The Kahn reaction of the blood was negative The urine was normal The electrocardiogram reveals myocardial damage Histologic sections from the mass in the cheek are presented

DISCUSSION

DR OLIVER S ORMSBY I saw one of those cases in my early experience It was only the second case that had been seen in this country My co-workers and I were fortunate enough to get a section which showed the typical sievelike arrangement where the paraffin entered the connective tissue This woman was very handsome, and she decided to have some dimples put in each side and to have some wrinkles taken out A half dozen large tumors developed A plastic surgeon removed them, and the result was very good At a later date we saw tumors from paraffin oil used for injection

DR S J ZAKON There are a lot of Romansky injections being given in the treatment of syphilis and other diseases with penicillin in large doses I have seen

the pedigree of a family in which some members had psoriasis, others arthritis and one member arthropathic psoriasis The peculiar observations of the biopsy of the joints will be reported by our orthopedic department In 1 case the verrucous lesions developed the second time around healing psoriatic lesions

Eosinophilic Granuloma Presented by DR EDWARD A OLIVER and (by invitation) DR E LORANT

M E C, a white man aged 42, first noticed a few reddish lesions on his face in January 1943 The lesions developed slowly, and the patient was kept under observation in a Naval dispensary A biopsy was performed in September 1943 and another in March 1944 On both occasions the diagnosis on pathologic examination was "chronic inflammation, probably mycosis fungoides"

From October to December 1943, he had eight roentgen irradiations at weekly intervals, of 75 r each After completion of the irradiations the lesions flattened and changed color from cherry red to pinkish brown However, three months after the roentgen therapy was completed the lesions became active again and have shown occasional activity to date

The patient now shows a quarter-sized lesion on the left cheek, another irregularly shaped quarter-sized lesion on the right cheek and a larger lesion in front of the right ear on the temporal region These lesions are nonelevated and reddish brown and are yellowish brown on pressure with a diascope They are not pruritic

The general physical examination and roentgenograms of the chest, feet and hands showed no evidence of pathologic changes

The urine was normal Examination of the blood showed a hemoglobin content of 87 to 90 per cent, a color index of 0 9, an erythrocyte count of 4,500,000 to 4,600,000 and a leukocyte count of 6,000 to 9,600, with a differential count of 48 to 56 per cent neutrophils, 38 to 46 per cent lymphocytes and 6 per cent eosinophils The sedimentation rate was 2 to 4 mm per hour The total protein was 6 9 mg per hundred cubic centimeters of blood, with an albumin-globulin ratio of 1 7 to 1

In a recent biopsy histologic observations were as follows The epidermis was uniform and apparently not increased in thickness There was slight hyperkeratosis The basal cells were well preserved, with a small amount of pigment present

In the corium completely separated from the epidermis there were large and small clusters of cells as well as cellular infiltrations composed of numerous lymphocytes, an occasional eosinophil, a few plasma cells and a few neutrophils were seen also The blood vessels and lymphatics were slightly dilated and presented occasional perivascular infiltrate There was slight edema throughout the corium The sebaceous and sweat glands were not especially involved

Histologic examination showed the epidermis to be normal In the middle portion of the corium, separated from the epidermis by a narrow band of normal connective tissue, lay a wide horizontal band of cellular infiltrate This cellular mass was densely packed, it was sharply circumscribed, and it included within its borders hairs and sebaceous glands There were many eosinophilic polymorphonuclear and mononuclear cells and many lymphocytes and histiocytes and fewer plasma cells

DISCUSSION

DR H M BULEY, Champaign, Ill During the past eighteen months my co-workers and I have had the opportunity to see several cases of eosinophilic granuloma of the skin representing various types of eruptions As has been stated in previous discussions, it is extremely difficult to find the common denominator for the various pictures presented in these cases I feel, therefore, that it is some-

a number of severe reactions in the buttocks following such injections The reactions would subside in a couple of weeks I wonder whether fifteen or twenty years from now one will see lesions similar to paraffinoma due to Romansky injections

DR STEPHEN ROTHMAN With vegetable oil and fatty acids paraffinoma does not occur Paraffinoma occurs exclusively with hydrocarbons I doubt whether white wax would produce paraffinoma, because such wax is composed of fatty acid

DR THEODORE CORNBLEET It is my feeling that one need not expect the same accidents to happen from the Romansky formula as from paraffin itself With paraffinoma there is no initial reaction, whereas with white wax one commonly finds a reaction in the tissues Originally, I tried to arrange to have a fluorescent light to detect the presence of the paraffin, which shows a Swiss cheese structure

Sporotrichosis Involving the Face and All Extremities Presented by DR MICHAEL H EBERT and (by invitation) DR N L BAKER

Dermatomycosis (?) Localized to Flexural Areas for Twenty Years Presented by DR H RATTNER and (by invitation) DR H RODIN and DR N L BAKER

Acute Disseminated Lupus Erythematosus in a Man Aged 37 Years Presented by DR MICHAEL H EBERT and (by invitation) DR N L BAKER

A Case for Diagnosis (Eruption Due to Drugs? Hemorrhagic Lupus Erythematosus? Toxic Purpuric Disease of Undetermined Origin?) Presented by DR S ROTHMAN and (by invitation) DR L RUBIN

Keratosis Follicularis (Darier?), Improved After Ingestion of Butter in Large Quantities Presented (by invitation) by DR H H RODIN

Recurrent Alopecia Areata Presented by DR E M SMITH JR

D D, a white boy, aged 7, rather small for his age, has a recurrent patch of alopecia areata involving the vertex and the strip down the center of his scalp toward the front This condition has occurred every September or October for the past five years and has run a course of about two or three months The configuration of hair loss is practically the same, and there is a complete clearing up of the condition between times

DISCUSSION

DR STEPHEN ROTHMAN I thought that definitely the boy had trichotillomania and that he had done a good job for himself

DR E M RUSTEN, Minneapolis I have a patient who is a resident in a tuberculosis sanatorium In 1928 he had pulmonary tunberculosis with bilateral effusion and rather extensive alopecia areata The pulmonary tuberculosis was controlled by sanatorium treatment, and he had a recurrence of hair growth About a year ago he had a recurrence of the pulmonary disease and again had alopecia areata His pulmonary disease is now improving, and his hair has also returned

DR JAMES R WEBSTER When I first saw the patient this afternoon I had the impression that the condition was trichotillomania, but on further examination concluded it was alopecia areata

what premature to suggest common causative factors, at least not until a larger number of case studies have been accumulated The case presented today is comparable to the case described by Pasini in 1940, and also with the case I presented here in November 1945 In these 3 patients the eruption started with macular erythema on the face, which within several months changed to a more or less extensive papular or nodular form Once the lesions reached their maximum size, however, they maintained their clinical appearance It is further remarkable that the disease did not interfere with the patients' general health No pathologic changes were found in either the lungs or the bones Although there was a slight increase in the eosinophil count of the blood the disease was essentially confined to the skin In all 3 cases the lesions were indolent, causing no discomfort to the patient In the patient presented today, relative lymphocytosis (30 to 40 per cent) was found, which, as far as I can recall, had not been noted in the other cases

DR CARL W LAYMON, Minneapolis There have been less than a dozen cases of eosinophilic granuloma of the skin in the literature, and the association of eosinophilic granuloma of the skin and bone is extremely rare The clinical picture of eosinophilic granuloma of the skin is subject to wide variations The lesions may be papules, nodules or plaques which are smooth or verrucous and usually red, purple or brown In the case recently reported by Dr Lewis and Dr Cormia there seemed to be an association between the eosinophilic granuloma and a fungous infection of the feet These observers suggestd that possibly eosinophilic grauloma of the skin might be linked to allergy of infection

DR EDWARD A OLIVER In this case the disease was difficult to diagnose clinically The patient stated that he had been treated in the Navy for mycosis fungoides He had received eight roentgen treatments I knew that it was not mycosis fungoides, and my first impression was that it was sarcoid Dr Caro then examined the sections for me, and his diagnosis was eosinophilic granuloma Dr Buley recently published an excellent article on eosinophilic granuloma in the December 1946 issue of the *Journal of Investigative Dermatology* This disease is most difficult to diagnose clinically because it occurs in so many different forms Only by a careful study of microscopic sections can one be sure of the diagnosis

Urticaria Pigmentosa of Recent Origin in an Adult, with No Mast Cells in the Section Presented by DR S J ZAKON and (by invitation) DR A L GOLDBERG

A Case of Urticaria Pigmentosa in a Child, with Mast Cells in the Corium. Presented by DR E A OLIVER and (by invitation) DR H F GARRARD

Preauricular Sinus Congenita (Bilateral) Presented by DR CLEVELAND J WHITE

Hyperplasia of the Gums Due to the Use of Dilantin® Sodium (Diphenylhydantoin Sodium) Presented by DR E M SMITH JR

DISCUSSION

DR ADOLPH ROSTENBERG JR (by invitation) Dilantin® is chemically closely related to the German drug nirvanol (phenylethylhydantoin) Van Wyk and Hoffmann (Periarteritis Nodosa, *Arch Int Med* **81** 605, 1948) pointed out the paucity of reactions seen with dilantin® and the large number seen with nirvanol, which is interesting considering the extremely close chemical relationship

DR FREDERICK R SCHMIDT At one time my co-workers and I collected 9 cases of alopecia areata which recurred regularly in September and March of succeeding years, which was apparently a type of arterial spasm, due to poor nutrition of the end arteries

DR E M SMITH JR It would be impossible for the patient to pull out the hair I have seen two recurrences, and they are absolutely the same, in that they run right down the middle of the scalp and extend only to the right side and not the left

Multiple Nevi (Adenoma Sebaceum) (Dermatosis Papulosa Nigra and Fibroma Pendulum) in a Negro Presented by DR E A OLIVER and (by invitation) DR E LORANT and DR A B HENNINGSEN

Lymphoblastoma Cutis with Poikilodermatous Changes Presented by DR F E SENEAR and STAFF

Ainhum of Two Years' Duration in a Negro Aged 66 Years Presented (by invitation) by DR MAURICE OPPENHEIM and DR DAVID COHEN

A Case for Diagnosis (Unilateral Vascular Nevus? Angioma Serpiginosum? Schamberg's Disease?) Presented by DR F E SENEAR and STAFF

Ichthyosiform Erythroderma? Presented by DR S ROTHMAN and (by invitation) DR J H MCCREARY

Localized Myxedema, Pretibial, Following Thyroidectomy Presented by DR F E SENEAR and STAFF

Probable Triple Symptom Complex of Behcet, Scrotal Tongue Presented by DR F E SENEAR and STAFF

A I, a white housewife aged 25, was shown at the December meeting of this society with a condition for diagnosis She gave a five months' history of recurrent ulcerative lesions of the mouth which had not responded to various local treatments or to intravenous treatment for a diagnosis of "trench mouth" made prior to admission At the time of presentation, she showed a marginal scrotal tongue with whitish patches of membrane extending from some of the crypts of the tongue, as well as scattered on the buccal mucous membranes These were relatively easily removed, leaving superficial tender ulcerations without bleeding and surrounded by an erythematous halo Direct examinations did not reveal mycelia During the discussion the following diagnoses were mentioned as possibilities (1) aphthous stomatitis, (2) moniliasis, (3) eruption due to drugs, (4) Behcet's triple symptom complex and (5) scrotal tongue

Medical consultation revealed nothing contributory The urine was normal, blood cell counts were normal, the results of the serologic test for syphilis and examination of the chest were all negative Examination by the gynecologic consultant showed only chronic cervicitis Repeated cultures from the mouth lesions failed to demonstrate Monilia, although cultures from vaginal discharge on one occassion did grow mucoid colonies with budding forms on microscopic examination On one occasion, the patient complained of soreness about the vulva,

DR S J ZAKON I wonder whether dilantin® is responsible for the hyperplasia or the poor oral hygiene of epileptic persons I had 1 case of this type which I referred to the dentist for oral prophylaxis, and the hypertrophy subsided in spite of the patient's taking dilantin®

DR STEPHAN ROTHMAN I saw a severe generalized hemorrhagic toxic eruption following the use of dilantin,® but the patient did not display hypertrophy of the gums

DR E M SMITH JR This patient was examined by several dentists, who readily agreed that the hypertrophy was a typical result of the long-continued use of dilantin® sodium and that such cases were moderately common in their experience

Dermatomyositis with Slightly Lichenified Lesions on Exposed Surfaces Presented by DR F E SENEAR and STAFF

Lymphocytoma Presented by DR O H FOERSTER, DR H R FOERSTER and (by invitation) DR D M RUCH

D E, a white woman aged 38, had a "pimple" on the right lateral aspect of the forehead in 1938 which she picked and scratched This became hard and raised and remained pea sized until 1945 Since then it has grown gradually, until it is now about four times its original size In 1942 a similar lesion appeared suddenly on the right side of the forehead above the original lesion, and in April 1946 a third similar lesion appeared lateral to the first one Neither of the latter two lesions have changed in size or appearance

On the right lateral aspect of the forehead, 2 cm above the lateral supraorbital margin, is a smooth, firm, cutaneous nodule, elevated about 4 mm Two similar round 5 mm lesions are also present, one 2 cm lateral to the former lesion and the other 0 5 cm above it

Histologic examination showed acanthosis to be present in some areas of the epidermis, and there was condensation in the collagen of the subpapillary layer Areas of lymphocytic infiltrates together with a few plasma cells were present about the glandular structures and in circumscribed areas deep in the corium

A blood cell count (March 18, 1947) showed hemoglobin 90 per cent, leukocytes 7,870, erythrocytes 4,590,000 and color index 1 00 The differential count showed 65 per cent neutrophils (2 per cent nonsegmented and 63 per cent segmented), 2 per cent eosinophils, no basophils, 30 per cent lymphocytes (large 1 per cent, small 29 per cent) and 3 per cent monocytes The blood smear was normal

DISCUSSION

DR M R CARO This patient presents a condition which is difficult to diagnose clinically 'The most obvious diagnosis clinically would be sarcoid, but on histologic examination these small accumulations of lymphocytic cells without any inflammatory reaction are diagnostic for lymphocytoma In the cases reported in the literature there are no observations in the blood stream to make this condition of more serious prognosis I recall a patient presented about ten years ago before this society with a lesion under the eye identical with that in the present case The lesion disappeared after three or four fractional doses of roentgen rays without any recurrence

DR ADOLPH ROSTENBERG JR (by invitation) In the eleventh supplement to 1943 Acta dermato-venereologica there is an article on lymphadenosis benigna cutis There is a fine English summary In lymphadenoma there are two varieties,

and examination in our department revealed superficial ulcerations about the labia minora and majora

On about the first of February, the patient was found to have decided injection of the right conjunctiva diagnosed as episcleritis by the ophthalmologic consultant This was considered consistent with, though not diagnostic of, Behcet's syndrome of the eye She stated that she had had one previous similar, though less severe, attack of ocular inflammation about five weeks ago

Perniones and Livedo Reticularis in a Poliomyelitic Limb Presented by Dr F E Senear and Staff

DISCUSSION

Dr M R Caro The sections were not typical of tuberculosis or tuberculid, though there were round cells which extended deeply into the fat

Dr Stephen Rothman I was very much impressed with this case because I saw quite a few after World War I in patients who had nerve injuries It shows what a profound effect trophic ulcers have on vasomotor action

Dr J F Madden, St Paul In our experience with poliomyelitis, my co-workers and I have noted that the patients have more cutaneous changes than the normal person During the acute stages in which the Sister Kenny method of therapy is used the patient often shows milaria from the hot applications

Dr F E Senear When I first saw this patient a couple of weeks ago, I thought that he had an exaggerated example of erythrocyanosis frigida crurum that the English have written about This is the first time I have seen one with so much inflammatory element that it simulated erythema exfoliativa Dr Brunner called our attention to the fact that Telford had pointed out that just this type of reaction does occur, particularly in the wasted limbs of persons who have had poliomyelitis I think, as Dr Rothman indicated, that it is a nerve injury that predisposes to this type of reaction, which is less intense than erythema exfoliativa

Eosinophilic Granuloma? Presented by Dr S Rothman and (by invitation) Dr J H McCreary

Since the age of 2 years, the patient, an 11 year old white girl, has been almost continuously sick with swelling of lymph nodes and with ulceration of the overlying skin on the head, neck and thorax The appearance of each new lesion has been accompanied with a temperature of 99 to 104 F, pain, tenderness, erythema and some swelling over the affected gland The overlying skin became red and shiny until spontaneous rupture occurred A seropurulent exudate appeared, and a crust was formed over a deep crater After rupture of the "abscess," the systemic symptoms disappeared and the temperature returned to normal There is a tendency toward slow healing with granulation and scar formation Since an operation two years ago for the removal of a group of cervical glands, the motion of the shoulders and neck has been restricted because of pain

Just previous to the onset of the present illness, the patient had measles and mumps at the same time During this illness the adenitis of the right submaxillary glands developed This adenitis failed to resolve, and formed an ulcer which persisted over twenty months Abscesses of nearby nodes followed in a similar characteristic course

Roentgen therapy seemed to accelerate healing, with remissions of the symptoms for as long as a year Dosages of the many courses of roentgen rays she received

in one there are isolated lesions such as this patient apparently has In the other variety there are multiple lesions, but in both the prognosis is about the same There is rarely systemic involvement An isolated cyst as this can arise at any age, whereas the generalized disseminated form is more often in elderly persons The author expressed the belief that a variety of stimuli are etiologic

DR HARRY FOERSTER, Milwaukee We presented this patient chiefly because of the frequency with which lesions of this type are misdiagnosed when they are not subjected to histologic study When first seen by us, the nodules appeared nevoid The history of progressive growth with appearance of new lesions in recent years, one as recently as nine months ago, suggested the possibility of endothelioma Sarcoid and sarcoma were also considered

Dr Caro made the diagnosis of lymphocytoma and also prepared the sections that were shown here today This patient received roentgen treatment about six weeks ago, and the lesions have been reduced about one third in size The pigmentation noted was caused or intensified by the roentgen therapy At the time this patient was being studied, we saw a woman with a similar lesion, and in the same site, which was shown to be an endothelioma on histologic examination

Albright's Syndrome (Fibrous Dysplasia of Bone, Precocious Puberty and Café au Lait Spots) Presented by DR F E SENEAR and STAFF

Francis W Lynch, M D, *President*

Leonard F Weber, M D, *Secretary*

April 16, 1947

A Case for Diagnosis (Streptococcic Eruption on the Face? Seborrheic Dermatitis?) Presented by DR JAMES HERBERT MITCHELL and (by invitation) DR ROBERT M GOODWIN

Pulsating Hemangiomas, Hepatic Cirrhosis Presented by DR T CORNBLEET and (by invitation) DR H SCHORR and DR J GRAFFIN

C D, a white woman aged 52, entered a medical ward at the Cook County Hospital on March 10, 1947 At this time she was given the diagnosis of cirrhosis of the liver with jaundice and ascites She was unable to give a history concerning the dermatitis of her forearms or the telangectatic lesions of her hands and face

Examination reveals a pulsating split-pea-sized lesion in the center of telangectasia on the right cheek The dorsum of the left hand has four smaller pulsating hemangiomas with a keratotic surface Both forearms and lower legs have a fairly well defined dermatitis The abdomen and chest show prominence of the superficial veins, and there are numerous telangiectases There is moderate ascites and icterus of the scleras Her temperature, while in the hospital, has steadily dropped from 102 to 99 F

The Kahn reaction of the blood was negative Repeated urinalyses revealed only a pronounced urobilinogen content The examination of the blood showed hemoglobin 58 per cent, erythrocytes 3,100,000 and leukocytes 8,100 The icterus index was 25 and 14 units The total protein was 6 1 Gm per hundred cubic centimeters, albumin 16 and globulin 4 5

The result of the cephalin flocculation test was 4 plus The nonprotein nitrogen was 31 mg per hundred cubic centimeters

so far are unknown to us Treatment with penicillin and sulfonamide drugs have had little effect on the course of the disease

The nodes have a tendency to mat together The ulcers are variable in size and shape, from 2 to 5 cm in diameter, and have a soft undermining edge and irregular granulating bases, well vascularized Some of the ulcers have appeared over regions where large lymph nodes are not usually present On the roentgenogram of the skull there is an irregular, oval dehiscence of the right parietal bone under one of the tender swellings The spleen is palpable The liver is felt at the costal margin

The axillary lymph node, seen on Jan 30, 1947, was a large moderately firm node of a peculiar red-brown The microscopic sections showed a very extensive obliteration of the normal architecture, although small remnants of cortical follicles and cords filled with lymphocytes remain These are widely separated and are missing from some parts of the node Instead one finds sheets of large acidophilic or pale nonfoamy macrophages, which seem to have filled in the sinuses as well as the parenchyma Scattered in great abundance between them are eosinophils and smaller dark cells which are presumably lymphocytes In some regions the cells with dark nuclei look more like normoblasts The histiocytes or macrophages frequently have lobulated nuclei, and sometimes they contain two or more discrete nuclei Neither in their cytoplasm nor in their nuclear form do they resemble Reed-Sternberg cells They do not possess distinct nuclei as shown in Mallory connective tissue stain, there is great fibrous thickening of the capsule and decided fibrosis of some of the cell-filled lymphatic sinuses Fibrous tissue is especially dense around the blood vessels of hilar portion of the node Evident in Mallory stain more clearly than in hematoxylin and eosin is the presence of clefts or small vacuoles of the cytoplasm of the large macrophages However, the appearance is quite different from that seen in the large cells of Gaucher's disease, in Niemann-Pick's disease or in Hand-Schüller-Christian's xanthomatosis Stains for gram-positive and acid-fast bacteria were entirely negative Sudan stain reveals an occasional macrophage containing recognizable septums A very small amount of this lipid is antisotrophic

The scraping of the sinus tract consists of multiple bits of granulation tissue and fragments of skin which show changes similar to those of the lymph nodes In the section of the skin the eosinophils are less prominent Plasma cells and large mononuclear cells are present The disease has been diagnosed once as tuberculosis by smear examination, and at another time as Hodgkin's disease by lymph node examination

In our laboratory tests, culture of the exudate on blood agar and Sabouraud's medium showed Staphylococcus albus The acid-fast stain was repeatedly negative Blood culture was negative White rat and guinea pig inoculations were repeatedly negative, results of the tuberculin patch test, blastomycin test, histoplasmin skin tests and purified protein derivative tests were all negative The Kahn reaction of the blood was negative Sternal puncture showed the myeloblast-erythroblast ratio to be elevated Other observations were sedimentation rate 41 mm in 1 hour, leukocytes 12,000, hemoglobin 12 Gm, erythrocytes 4,400,000, poloymorphonuclear cells 72 per cent, lymphocytes 26 per cent, eosinophils 2 per cent, hematocrit 41 and blood lipids 787

The histologic section from a lymph node presented a very unusual appearance which did not resemble any lymph node previously studied in our laboratories Certainly tuberculosis and Hodgkin's disease in their usual forms can be excluded On anatomic evidence at present, we have no clue as to whether this peculiar

DISCUSSION

DR S J ZAKON The internists recognize this as part of the signs and symptoms of the Chvostek Habitus (Chvostek, F Cirrohis of the Liver, *Wien Klin Wchnschr* **35** 381, 1922), in which there are ascites and jaundice, pulsating spider nevi and loss of body, axillary and pubic hair This is usually observed in nonobstructive jaundice

DR HAMILTON MONTGOMERY, Rochester, Minn My co-workers and I have seen a number of pulsating hemangiomas of the skin in patients referred by various internists in our clinic Dr Williams and Dr Snall reported a series of these cases (*Arch Int Med* **62** 872-882 [Nov] 1938) All the phenomena that have just been mentioned are not necessarily present Pulsating hemangiomas are almost invariably associated with cirrhosis of the liver

DR THEODORE CORNBLEET At the Cook County Hospital various clinicians have pointed out for years that there is a lack or sparsity of hair about the male abdomen and chest in the presence of cirrhosis of the liver My associates and I always suspect that there is cirrhosis of the liver in such cases In a number of these patients telangiectases of the chest and upper part of the abdomen and a few of the blood vessel enlargements can be seen, or more often felt, to pulsate We have tried the newer nutritional remedies for cirrhosis of the liver, such as methionine and cysteine Though some of those patients were said to be improved clinically and show better results in tests of hepatic function, I have never seen these angiomas and telangiectases disappear thereby I have seen these lesions regress, however, after parturition There is no doubt that in other cases they may clear spontaneously

A Case for Diagnosis (Lupus Erythematosus, Telangiectatic Type?) Presented by DR CLEVELAND WHITE and (by invitation) DR J L MADURA

Squamous Cell Carcinoma of the Penis Presented by DR M OPPENHEIM and DR D COHEN

Mr C P, a Negro aged 49, has a tumor-like lesion on the penis of four years' duration There is no pain but some tenderness on pressure The lesion is about the size of a half-dollar and is situated on the outside of the prepuce It has an irregular configuration, in some places polycyclic with overhanging margins There are yellowish crusts and scales on the surface When these are removed, pressure on the tumor cause white millet-sized drops to appear The lesion is indurated and of a cartilaginous consistency There is no inflammation Inguinal glands are not enlarged

On the glans penis there are depigmented, depressed, irregular scars with a smooth flat base and a slight hyperpigmentation in the periphery This lesion began as a solid nodule four years ago (1943) and has progressed until the present time In 1943 and in 1917 the patient received treatment for his blood For many years he was a laborer on a railroad, and now he is employed in an ice cream factory. No history of exposure to oil is given

The urine is normal The blood cell count is normal The Kahn reaction of the blood was negative on April 19, 1947, and on April 20, 1947

Biopsy of the skin reveals acanthosis, mainly limited to the large rete projections The prickle cell layer is growing atypically Little mitosis is present There is a dense lymphocytic infiltration in the dendritic ramifications of the papillary layer

granulomatous condition is an infection or is caused by a metabolic anomaly It more closely resembles the tissue reaction seen in eosinophilic granuloma of bone than any other condition known to us

DISCUSSION

DR CARL W LAYMON, Minneapolis There is not a great deal known about eosinophilic granuloma of the skin, since not more than a dozen cases have been reported and in those cases the diagnosis was doubtful The disease has been reported in nodules or plaques which brings up the interesting question as to whether cutaneous eosinophilic granuloma is related to eosinophilic granuloma in the lung and other organs That brings up a possible relation to Christian's disease I believe that all of these diseases are part of the same toxic process and that this occurs as a fatal type and the Christian type occurs as a more benign disease Cutaneous eosinophilic granuloma and eosinophilic granuloma of the bone are part of the same process Last April, at the meeting in Detroit, Dr Curtis showed a patient with eosinophilic granuloma of the bone with cutaneous lesions

DR A C CURTIS, Ann Arbor Experience in 1 case does not make one an authority The patient that Dr Laymon mentioned had plaquelike lesions on the vulva and one lesion on the scalp, with a destructive process in the bone of the mastoid and in the crest of the ilium The lesions were plaquelike and very red Our attention was called to them because of the redness They promptly disappeared with a minimal amount of low voltage roentgen rays, as did the destructive lesions in the bone As I looked through the records to see whether any studies had been made, it occurred to me that this might be a disseminated sporotrichosis

DR STEPHEN ROTHMAN The diagnosis of eosinophilic granuloma was first suggested by our pathologist, Dr E M Humphreys I realize that these cutaneous lesions have not been reported in the literature It does not agree with any description published in the literature It reminded me of Niemann-Pick's disease, but the pathologist said that it was not Clinically it was typical scrofuloderma Extensive examinations were made for fungi The patient was seen in several departments I think that we can by now exclude tuberculosis and mycosis

Calcinosis of the Elbows Presented by DR DAVID V OMENS and (by invitation) DR HAROLD D OMENS

Leukoplakia, Sublingual (White Sponge Nevus?) Presented by MAURICE OPPENHEIM and (by invitation) DR WILLIAM A YACULLO

Pityriasis Rubra Pilaris in a Five Year Old Presented by DR MARCUS R CARO and (by invitation) DR LAURENCE L PALITZ

Parapsoriasis Guttata, with Unusually Small Lesions Presented by DR EDWARD A OLIVER and (by invitation) DR E LORANT and DR A B HENNINGSEN

A Case for Diagnosis (Psoriasis? Lupus Erythematosus?) Presented by DR ALBERT H SLEPYAN (by invitation)

DISCUSSION

DR S J ZAKON About two weeks ago I saw a man with carcinoma of the penis which had been treated for syphilis for some time I reviewed the literature, which is mostly in the field of urology (Melicow, M M, and Ganem, E J Cancerous and Precancerous Lesions of the Penis, *J of Urol* **55** 486, 1946) Early diagnosis is advised because of the serious prognosis It is interesting that there has never been a report of a case of carcinoma of the penis in a Jew, not because of any racial immunity but because of early circumcision In the Mohammedans, who circumcise their children at the age of 13, there is a definite incidence of carcinoma of the penis With early diagnosis some patients will recover In the far advanced case, even with radical amputation and removal of the regional glands, the prognosis is poor

DR THEODORE CORNBLUTH In a recent communication of *Science* (**105** 391 [April 11] 1947), Plant and Kahn-Speyer mention that carcinoma of the penis does not occur in persons who have been circumcised in the first few weeks of life and is rare in those who have been circumcised in childhood or in early puberty This induced them to study the carcinogenic action of smegma in mice using material obtained from horses Their work was evidently done carefully with suitable controls and showed that smegma is carcinogenic

This man's lesion was not highly characteristic for carcinoma of the penis, though that diagnosis is probably correct Epitheliomas at this site are usually of the squamous cell type and highly malignant Yet the present lesion began four years ago and the regional lymph glands are not enlarged

DR HAMILTON MONTGOMERY, Rochester, Minn I do not believe that this is an epithelioma histologically There are well defined pearls but few mitotic figures The cells are edematous and large, and there is an area of parakeratosis I think that this is a condyloma acuminatum and not an epithelioma As brought out by the first discusser, epithelioma of the penis usually grows rapidly except those that start on the foreskin In cases in which there is a so-called precancerous stage, moist leukoplakia or erythroplasia, simple circumcision is often enough to prevent the lesion from becoming a frank epithelioma I do not believe that in this patient amputation of the penis will be necessary

DR STURE JOHNSON, Madison, Wis (by invitation) I wonder whether the disease might be histoplasmosis At Ann Arbor, Mich, I saw 2 patients with lesions of histoplasmosis of the genitalia By careful search my co-workers and I were able to demonstrate the organisms in the tissues Schaeffer and his group have also reported cases in which the lesions were present on the genitalia Genital involvement with Histoplasma capsulatum is not unusual The organisms are usually difficult to detect in tissue and to culture I should like to call attention to two articles with photographs of genital histoplasmosis one by Palmer, Almolsch and Shaffer (ARCH DERMAT & SYPH **45** 919 [May] 1942) and the other by Curtis and Cawley (*J Urol* **57** 781 [April] 1947)

DR MAURICE OPPENHEIM (by invitation) The site of this epithelioma is unusual It is not the favorite place The favorite site for carcinoma of the penis is on the inside and on the glans The striking thing is that it has taken four years for it to grow to this size

I do not agree with Dr Montgomery that the histologic observations are atypical with few mitotic figures There is a decided inflammatory reaction surrounding the atypical epithelial growth This carcinoma looks like the so-called mule-spinner cancer, which is produced by lubrication oil used in cotton mills in England and Scotland

Necrobiosis Lipoidica Diabeticorum, Lesions on the Legs Presented by Dr S Rothman and (by invitation) Dr Z Felsher and Dr L Rubin

Linear Scleroderma Presented by Dr S Rothman and (by invitation) Dr H Krysa

Nevus Unius Lateris with Chronic Inflammation? Presented by Dr S Rothman and (by invitation) Dr E L Laden

Marcus R Caro, M D, *President*

Leonard F Weber, M D, *Secretary*

March 19, 1947

Lichen Sclerosus et Atrophicus and Rosacea with Acne and Rhinophyma in a 49 Year Old Woman Presented by Dr D Omens and (by invitation) Dr H Omens and Dr J Graffin

Lichen Simplex Chronicus of the Vulva of Three Years' Duration in a Seven Year Old White Girl Presented by Dr David V Omens and (by invitation) Dr H Omens and Dr N L Baker

Mycosis Fungoides d'Emblée Presented by Dr D Omens and (by invitation) Dr H Omens and Dr N L Baker

A Case for Diagnosis, Postinflammatory Cystic or Keloidal Lesions of the Hands Presented by Dr H Rattner and (by invitation) Dr J Graffin

A Case for Diagnosis (Actinomycosis? Ecthyma?) Presented by Dr M H Ebert and (by invitation) Dr J Graffin

Widespread Cutaneous Nodular Sarcoidosis with No Systemic Manifestations Presented by Dr H Rattner and (by invitation) Dr Rodin and Dr J Graffin

Classic Acrodermatitis Chronica Atrophicans with Involvement of the Palms, Atrophy, Pseudosclerodermatous Plaques and Fibromas Presented by Dr M Ebert and (by invitation) Dr V Leaf and Dr J Graffin

Generalized Argyria from the Ingestion of Argyrol, One Ounce a Week for Five Years, to Prevent "Colds" Presented by Dr M Ebert and (by invitation) Dr J Graffin

Bizarre Pigmentation, Cause Undetermined in a Pituitary Type Dwarf Presented by Dr T Cornbleet and (by invitation) Dr D Cohen and Dr N L Baker

Against the diagnosis of condyloma acuminatum are the hard consistency, the broad base and the smooth surface The unusual factor is that these cancers are of long duration without metastases to lymph nodes

Epidermodysplasia Verruciformis Presented by DR MARCUS R CARO and (by invitation) DR LAURENCE L PALITZ

B G, a white girl aged 16, first had cutaneous lesions on the wrists and ankles at the age of 10, with gradual extension to the present distribution There was some improvement each summer, but the lesions never disappeared, there were no subjective symptoms There was no history of parental consanguinity

On the dorsal surface of the hands are patches of erythematous, raised papules with verrucous surfaces On the left hand these papules extend across the outer side of the thumb to involve the volar surface of the thumb for a short distance On both hands they extend around the ulnar side of the wrists to the flexor surface and then along the ulnar part of the flexor surface of the forearms to the cubital fossae There is a diffuse patch of erythematous and slightly hyperkeratotic dermatitis about the right axilla and also on the inner surface of the right arm There are also difluse lichenified patches on the outer surface of the hips, more on the right side, and on the outer surface of the right knee, while on the front of the left knee are many small warty papules On both insteps are many pea-sized, warty papules, which extend upward to the dorsal surface of the feet, across both ankles and along the outer side of the feet A few papules are present on the dorsal surface of several toes The skin is erythematous about the papules on the feet and ankles There is also diffuse acne on the forehead, which has improved with the use of 30 per cent sulfur paste The verrucous lesions have remained unchanged with local treatment and the administration of vitamin A and paraaminobenzoic acid

Histologic examination of a biopsy specimen from the left wrist showed a thick scale in which the cornified layers were interlaced Nuclei were absent except in one small area of parakeratosis The epidermis showed irregular acanthosis except for thinning beneath the parakeratotic scale At this site the granular layer was missing Elsewhere the granular layer was thickened, and in some cells there were small vacuoles The corium was edematous, and it contained a diffuse infiltration of lymphocytes, histiocytes and connective tissue cells In many places the edema and cellular infiltrate extended up into the epidermis, and the demarcation between the epidermis and corium became indistinct The Weigert stain showed the elastic fibers to be entirely missing from the upper part of the corium

DISCUSSION

DR HAMILTON MONTGOMERY, Rochester, Minn I would agree that this is an epidermodysplasia verruciformis clinically, but the histopathologic picture shows none of the features of this disorder, especially there is no evidence of vacuolization of the cells in the granular layer This histologic picture is more that of acrokeratosis of Hopf Histologically one might regard the condition also as a form of delayed epithelial nevus, using this term in the broadest sense

DR. MARCUS R CARO I think that clinically this case fits in essentially with the description of the disease in the literature Histologically it must be granted that there is here less vacuolization in the granular layer than has been described I recall also that in a patient shown before this society by Dr Weber (ARCH DERMAT & SYPH **49** 217, 1944) there was some variation from the classic picture I wonder whether we are not trying to classify the disease in these cases

dermatologic service the patient should be isolated I am sure that I have seen the infection carried by and transferred by attendants

Tuberculosis Colliquativa of the Sternum in an Eleven Year Old Negro Girl Presented by DR D V OMENS and (by invitation) DR H OMENS and DR B YAFFEE

Generalized Acne Scrofulosorum, Ecthyma Presented by DR F E SENEAR and STAFF

R S, a 4 year old Negro boy, was admitted to the Illinois Research and Educational Hospitals for the treatment of tuberculosis of the right hip For six months a generalized eruption had been present and large ulcerations had appeared on both legs

Examination revealed numerous folliculopapular lesions distributed over the entire cutaneous surface but most concentrated on the extensor surfaces of the extremities A few lesions exhibited central necrosis, older lesions were represented by slightly depressed scars, depigmented at the centers and with hyperpigmented borders A fading eruption of tiny lichenoid papules was present on the sides of the trunk Large granulating ulcers were noted over the anterior aspects of both legs

A bullous reaction developed after skin testing with 1 10,000 old tuberculin The report of biopsy is not yet available

DISCUSSION

DR H E MICHELSON, Minneapolis It has never been clear to me why certain types of tuberculosis respond to roentgen therapy and others do not For example, bone and most skin lesions do not respond while glandular tuberculosis and certain peritoneal types do There are many other facts about glandular tuberculosis that are most interesting, especially the seasonal incidence One does not see many patients with generalized tuberculous eruptions Recently Schmidt wrote a good article on these eruptions in the German dermatology journal (*Archiv für Dermatologie und Syphilis*)

Dermatitis in Red Area of Tattoo, Reaction Positive to Patch Test with Ammoniated Mercury, Negative with Cinnabar Presented by (by invitation) DR EVERETT T DUNCAN and DR CLARK F JOHNSON

Psoriasis Verrucosa, Arthropathy and Koebner's Phenomenon Presented by DR S ROTHMAN and (by invitation) DR J MCCREARY

DISCUSSION

DR MARY S SHERMAN It is variously estimated that 2 to 4 per cent of patients with symptoms of chronic arthritis have psoriasis Conversely up to 12 per cent of patients with psoriasis may be expected to have joint symptoms at one time or another Since the joints are rarely involved severely enough so that operation is indicated, reports of the pathologic changes are few

The clinical characteristics of so-called psoriatic arthritis are well known Males are affected more than females Although any joint or combination of joints may be involved, the joints most commonly and characteristically troublesome are the terminal interphalangeal joints of fingers and toes, and there are usually associated typical nail changes It is especially noteworthy that the joint

manifestations do not respond to treatment directed toward the arthritis, but improve miraculously as the cutaneous lesions subside

As a rule, therefore, the arthritic manifestations subside between exacerbations of the cutaneous lesions and in the intervals there are usually no symptoms of permanent residual damage Occasionally the joints are irritated sufficiently so that they do not return to normal, and there have been reports of complete ankylosis

In the present case arthritic symptoms appeared at the early age of 17, one and a half years after the onset of the cutaneous disease The psoriasis was essentially untreated and grew progressively worse During the next two and a half years, more and more joints became involved, and none of them improved The patient had been completly incapacitated by the pain in his knees

The roentgenograms of this boy's knees show little other than regional atrophy and beginning degenerative changes The cartilage space is well preserved, but there is irregularity of the articulating surface of the patella and small osteophytes forming at its periphery The roentgenograms of the hands show more typical changes In the right hand the terminal two joints of the fifth finger have been largely destroyed and marginal absorption of the ends of the phalanges is evident. In the left hand similar changes are observed in the terminal joint of the long finger and in all the joints of the index finger In the metacarpophalangeal joint there has been peripheral destruction of the articular cortex, so that only the central portion is visible

When biopsy of the right knee joint was undertaken, the cutaneous lesions had begun to show some improvement Exploration of the knee joint revealed gross damage There was severe synovitis which had resulted in dense adhesions The synovial membrane had grown over the joint surfaces, so that the tibia was scarcely visible The patella was encircled by numerous osteophytes and its articular cartilage was completely destroyed except for a few soft gelatinous remnants What was visible of the surfaces of the tibia and femur appeared to be normal This first section is from the synovial membrane It shows the grossly hypertrophied villi The most striking change is the great amount of well organized, vascular, fibrous thickening, with relatively few signs of inflammation, an observation which was noted by Bauer and his associates The blood vessels are also somewhat sclerotic This is in contrast to the chronic inflammatory character of this synovial membrane taken from a patient with Still's rheumatoid arthritis

A piece of bone and cartilage was removed from the edge of the femoral condyle in an area where the articulating surface looked normal, but the section reveals advanced changes No articular cartilage remains It has been entirely replaced by a collagenous type of fibrocartilage which contains numerous blood vessels Beneath the cortex is seen a sort of chronic granulation tissue Between these two the bony cortex has been thinned to a narrow plate, which in one spot is almost disrupted

It is, of course, not possible to say whether these changes are characteristic of psoriasis They are certainly not like those one associates with rheumatoid arthritis In fact, they are not quite like any of the known chronic arthritides It will take further study before we understand how this appearance is produced and what it means

Psoriasis Verrucosa, Developing During Treatment Presented by DR S ROTHMAN and (by invitation) DR L RUBIN

DISCUSSION

DR STEPHEN ROTHMAN The relationship between psoriasis and arthropathia according to Julius Bauer is due to debility of conjugated genes He published

on the basis of criteria that are a little bit too rigid I think that the lesions in all of these cases are forms of tardy epithelial nevi

A Case for Diagnosis Presented by DR FRANCIS E SENEAR

M S, a woman aged 75, was seen with an eruption on the arms and legs which had been present constantly for the past five years, without any appreciable change except for extension in recent years There are no symptoms The patient states that she was seen at the Billings Clinic some years ago and that a diagnosis of purpura was made She has been seen by a number of other physicians, and a variety of diagnoses have been suggested

Biopsy shows a slight degree of intracellular edema of the epidermis with liquefaction degeneration of the basal layer in several places At these sites the blood vessels were dilated and were surrounded by a loose infiltrate of lymphocytes and erythrocytes, some of the cells extending up to the basal layer Perl's prussian blue reaction did not show any iron pigment

A Case for Diagnosis (Idiopathic Multiple Hemorrhagic Sarcoma [Kaposi] or Pigmented Purpuric Lichenoid Dermatitis?) Presented by DR O H FOERSTER and DR H R FOERSTER and (by invitation) DR D M RUCH

V S, a man aged 28, is presented because of an eruption on his lower legs, feet and toes of three years' duration He stated that in 1944 the dorsal and lateral surfaces of his great toes showed a red-brown discoloration and elevated lesions The condition remained localized until January 1946, when it extended to the dorsal surfaces of his feet and toes and to the lateral surface of each ankle In June an apparent ulceration appeared on each side of his right ankle These open lesions healed in October 1946 The eruption was first observed on his lower legs in November 1946

Examination discloses a red-brown lichenoid, diffuse, small papular eruption in patches on the sides of the first three toes of the left foot and the first four toes on the right foot, the dorsal surfaces of the feet, at the bases of the toes the heels, ankles and the anterior and medial surfaces of the lower legs directly above the ankles

The result of the Rumple-Leeds test was negative Intradermal and subcutaneous tests with congo red elicited negative reactions for amyloid

The examination of the blood showed erythrocytes 6,530,000, leukocytes 12,750 hemoglobin over 18 Gm, thrombocytes 350,000, clot retraction time 1 hour and 20 minutes, coagulation time 10 minutes and 30 seconds and bleeding time 3 minutes and 30 seconds

The histologic examination of a section taken from the dorsal surface of the right foot adjacent to the toes showed moderate hyperkeratosis and a normal epidermis There was proliferation of the walls of all the vessels of the cutis A moderately dense lymphocytic infiltrate was present in the upper and middle parts of the cutis The iron stain showed a large amount of hemosiderin in the cutis

DISCUSSION

DR HAMILTON MONTGOMERY, Rochester, Minn In Foerster's case, it was difficult to make a histologic diagnosis The section showed proliferation of capillaries and some of the smaller venules Some of the capillaries were open ended, as one sees in Kaposi's sarcoma There were also apparently some lymphocytoid cells of Marchand Against a diagnosis of Kaposi's sarcoma was the diffuse uni-

sarcoidosis, much as Dr Rothman presented today, where there was involvement of bone, lymph glands and skin We have studied the cases extensively by biopsy, chemical studies and roentgenogram In this series, to be presented before the Society of Investigative Dermatology, many showed striking improvement with vitamin D_2 and dihydrotachysterol therapy

DR STEPHEN ROTHMAN I agree with Dr Curtis that sarcoid structure has a multiple etiology, sarcoid leprosy, sarcoid syphilis and foreign-body sarcoids being important examples Still, there is a rather well defined entity of "sarcoidosis" with characteristic involvement of skin, bone, eyes and lungs, and evidence is accumulating that this disease is of tuberculous origin The "positive anergy" to tuberculin and the tuberculin-neutralizing properties of the blood serum are present in such high percentage in our material that it must be regarded as highly characteristic for this condition

DR ARTHUR C CURTIS I did not intend to leave the impression that sarcoidosis is not a clinical entity I think that it is Nor did I mean that silica or a foreign body reaction is a common cause of sarcoidosis There are some cases in which it may be the etiologic factor

Familial Keratosis Pilaris with Monilethrix-like Anomaly of the Hair in Fourth Generation, Maternal Side Presented by DR S ROTHMAN and (by invitation) DR R J STANWOOD

Dermatitis Herpetiformis Potentiated Effect of Pyribenzamine-Sulfapyridine Combination Presented by DR S ROTHMAN and (by invitation) DR J H MCCREARY

DISCUSSION

DR STEPHEN ROTHMAN In this case tripelennamine hydrochloride (pyribenzamine®) acts not because it is an antihistaminic drug, but because it contains the pyridine nucleus The therapeutic result in this case has been strikingly good

DR ZACHARY FELSHER (by invitation) There seems to be a relation, at least in some cases of dermatitis herpetiformis, between the presence of the pyridine group in the drug and its beneficial action In 2 of our cases of dermatitis herpetiformis both nicotinamide and pyridium® (phenylazo-alpha-diaminopyridine monohydrochloride) appeared beneficial Both drugs contain pyridine groups The disease in one of these cases was absolutely refractory to sulfapyridine, yet responded to nicotinamide and pyridium® In 2 other cases sulfapyridine caused complete clearing of the eruption, but nicotinamide and pyribenzamine® had no effect In a fifth case none of the pyridine-containing drugs worked at all I do not know the reasons for this discrepancy

In 1 of our cases of dermatitis herpetiformis which was completely controlled by sulfapyridine, 300 mg of paraaminobenzoic acid daily was given simultaneously to note whether this drug would interfere with the action of the sulfapyridine as it does in bacterial infections There was no interference with the beneficial action of the sulfapyridine Perhaps this points to the possibility that the action of sulfapyridine in dermatitis herpetiformis is different from its action in bacterial infections

DR ASHTON L WELSH, Cincinnati (by invitation) I did not see the patient under discussion, but I am interested in what has been said about the use of sulfapyridine in dermatitis herpetiformis In the last year my co-workers and I have treated a number of patients who had dermatitis herpetiformis with

form staining of the entire section with hemosiderin rather than a spotted deposition of hemosiderin There was no evidence of any tumor stage, such as fibrosarcoma I believe that this is probably an early stage of Kaposi's sarcoma both clinically and histologically One must bear in mind that Kaposi's sarcoma can progress slowly, just as mycosis fungoides may remain in an early plaque stage simulating parapsoriasis for a period of many years

DR STEPHEN ROTHMAN The patient presented by Dr Senear was seen in the University of Chicago Clinics by Dr Stenhouse and myself in 1943 At that time the tentative clinical diagnosis of Majocchi's disease with hypertension was made The biopsy specimen did not show extravasation of blood or blood pigment I believe that the eruption has not changed much in the last four years, and it is remarkable that the hypertension, too, is rather benign and stationary

Gottron in Germany stressed the point that Majocchi's purpura is always associated with either polycythemia or hypertension I do not know whether this has ever been confirmed, but the association of a widespread telangiectatic eruption with hypertension certainly is remarkable

DR F E SENEAR Several years ago I observed 2 cases, 1 patient was shown before this society and originally presented the somewhat mammalated appearance that this patient showed on the leg Histologically the lesions in both cases were typical of Kaposi's sarcoma

DR HARRY R FOERSTER, Milwaukee In our case we had considered the possibilities of Kaposi's idiopathic hemorrhagic sarcoma, amyloid disease and lichenoid pigmentary dermatosis and, on clinical grounds, decided in favor of the last named Dr Montgomery made a histologic diagnosis of Kaposi's sarcoma without having seen the patient MacKee and Cipollaro reported a case of Kaposi's sarcoma in which only inflammatory manifestations were present, which is in accord with Dr Webster's comment I am inclined to agree with him Our patient observed his first lesions three years ago These lesions were confined to the feet, particularly the dorsa of the toes, for almost three years In January 1946, the eruption extended to the dorsum of each foot and to the ankles, and during the last five or six months lesions have appeared on the legs Today he shows lesions that have developed since our first examination of him six weeks ago These lesions are more of a purpuric type The dark red in this case contrasts with the orange in Dr Caro's case, which I thought was an example of Schamberg's disease In Schamberg's or Majocchi's disease I have not seen the papular infiltrate exhibited by our patient, nor have I seen a case of Kaposi's sarcoma with so little infiltration I therefore favored a diagnosis of pigmented purpuric lichenoid dermatitis

Extensive Morphea Presented by DR S ROTHMAN and (by invitation) DR L RUBIN

Eosinophilic Granuloma Progress with High Voltage Roentgen Therapy Presented (by invitation) by DR M PIERCE and DR S ROTHMAN

Since this patient was presented originally at the Chicago Dermatological Society, in February 1947, further search for a positive agent in cultures from biopsy specimens, inoculation into guinea pigs and on bacteriologic mediums have failed to reveal the presence of an organism

On February 28, a biopsy of the skull lesion in the right parietal bone was made The histologic picture of this lesion was similar to that found in the granulomatous lymph node tissue The microscopic report was as follows The

sulfapyridine Several interesting observations have been made Apparently large amounts of sulfapyridine are usually unnecessary to control the reaction if pyribenzamine® is given simultaneously The 4 to 7 tablets of sulfapyridine daily can often be reduced to 1 tablet a day if pyribenzamine® is given at the same time It was our experience that pyribenzamine® alone has not been very helpful It has not been helpful in preventing the outcropping of skin lesions Another group of 10 patients who had dermatitis herpetiformis were treated with sulfapyridine and paraaminobenzoic acid simultaneously They were given as much as 100 mg of paraaminobenzoic acid daily We observed in only 2 of these 10 patients some inhibition of the action of the sulfapyridine In the other 8 there was no apparent inhibition of this action It appears that in dermatitis herpetiformis sulfapyridine has some action on the causative bacteria which is different from the action usually attributed to this drug on the bacteria involved in other diseases The paraaminobenzoic acid alone may have some favorable action in dermatitis herpetiformis, but to date we have not treated patients who had dermatitis herpetiformis with this drug alone This should and will be done to control the study already mentioned Suggesting some unusual action of the sulfapyridine on the bacteria in dermatitis herpetiformis is the fact that in many instances only 1 tablet daily, or 1 every other day, was necessary to control this problem This has not been an observation with this drug in other diseases

DR. ADOLPH ROSTENBERG JR (by invitation) I could not make a diagnosis of dermatitis herpetiformis In order to evaluate the therapeutic result one should be sure of the diagnosis I do not know that it was a papular eczema It started eight years ago

DR STEPHEN ROTHMAN Many of the outstanding New York dermatologists who saw this patient did not diagnose dermatitis herpetiformis because the patient displayed no vesicles However, after we had done a patch test with potassium iodide, the patient had a rather characteristic vesicular eruption Dr O'Leary saw the patient at that time and agreed with the diagnosis of dermatitis herpetiformis A few characteristic grouped vesicular lesions are still present

Kaposi's Sarcoma in a 50 Year Old White Man with Tumors on the Toes Presented by DR EDWARD A OLIVER and Dermatology Staff

A Case for Diagnosis (Exfoliative Dermatitis or Pityriasis Rubra Pilaris?) Presented by DR JULIUS E GINSBURG and (by invitation) DR I EIRINBERG

A Case for Diagnosis (Glossy Skin? Morvan's Disease? Possible Radio Dermatitis?) Presented by DR JAMES HERBERT MITCHELL and (by invitation) DR ROBERT H HARRIS

Generalized Mycosis Fungoides of Six Years' Duration Presented by DR EDWARD A OLIVER and Dermatology Staff

Acrodermatitis Chronica Atrophicans Presented by DR I M FELSHER and DR A SLEPYAN and (by invitation) DR I EIRINBERG

Alopecia Areata Totalis Associated with Hypothyroidism, Regrowth of Hairs Presented by DR S ROTHMAN and (by invitation) DR Z FELSHER and DR L RUBIN

tissue fragments were made up for the most part of large acidophilic or nonfoamy macrophages These had large irregular-shaped nuclei with indistinct nucleoli They contained a moderate amount of cytoplasm Many of these macrophages were binucleated, and there was some infolding of the nuclear membrane Scattered among these cells were a moderate number of eosinophils, more numerous in some of the fragments There were also a few smaller cells with dark nuclei, which presumably were lymphocytes There were a few multinucleated giant cells, some of these containing vacuoles or slitlike spaces A stain for fat (sudan IV) revealed that a moderate number of the macrophages contained small or moderate-sized fat droplets, or lipoprotein granules, most of which were not anisotropic Blood lipid studies showed no elevation of the total blood lipids or blood cholesterols

Therapy consisted of external irradiation, massage and physical therapy to correct the fibrosis in the cervical region Before admission to Bobs Roberts Hospital, the child had received a total of 2,593 r between Jan 13, 1939 and June 12, 1945 Since June 14, she has received forty-three treatments to seventeen cutaneous lesions, totaling 1500 r with single doses of 300 to 500 r She has experienced no radiation sickness She improved progressively The lesions are gradually regressing, and at present there are no discharging areas She has gained 27 to 30 Kg in weight since admission The retraction of her head has improved to some degree The patient is now to be discharged from the hospital and will be followed in the outpatient department

Eosinophilic Granuloma Presented by DR EDWARD A OLIVER and (by invitation) DR E LORANT

M E C, a white man aged 42, was presented at the March meeting He is presented today to show the effect of treatment

DISCUSSION

DR H M BULEY, Champaign, Ill (by invitation) These 2 cases illustrate again that there are various etiologic entities in eosinophilic granuloma In both cases there is symptomatic involvement which would not be present in many other cases The improvement following roentgen ray treatment is remarkable In the case I observed roentgen rays had no effect I saw the patient two weeks ago, and the lesions were practically as I saw them two years ago

DR ASHTON L WELSH, Cincinnati (by invitation) I wish to report further on the patient that my co-workers and I observed in Cincinnati, who was treated in the same fashion as this one His improvement was as striking as was the improvement in Dr Oliver's patient He now has fewer lesions, has gained weight and is considerably improved His spleen, which was palpable before roentgen therapy was begun, is still palpable but decidedly smaller The few small palpable lymph nodes that he had before roentgen therapy are still palpable and have been only slightly reduced in size They were chiefly around the neck and in one axilla We have been carefully watching this man, and I cannot help feeling that this syndrome is a little different from other forms of lymphoblastoma, if it is a lymphoblastoma, particularly in that the toxic or "id" reactions in this syndrome are so pronounced Low voltage roentgen rays administered to various skin areas in the man we treated produced little change, as in Dr Oliver's case

DR HAMILTON MONTGOMERY, Rochester, Minn Eosinophilic granulomas of the skin should be differentiated from eosinophilic granulomas of the skin and bone A series of articles appeared in the February 1947 issue of THE ARCHIVES Eosinophilic granuloma of the skin may be of various types, including pseudo

Acrodermatitis Chronicus Atrophicans Presented by DR JAMES HERBERT MITCHELL and (by invitation) DR ROBERT H HARRIS

A Case for Diagnosis (Sarcoid? Syphilis?) Presented by DR EDWIN M SMITH JR

Supernumerary Breasts in Axillas (with a Nipple [?] on One Only) Presented by DR I M FELSHER and DR A SLEPYAN and (by invitation) DR I EIRINBERG

Von Recklinghausen's Disease (Neurofibromatosis) Presented by DR FRANCIS E SENEAR and Staff

Prurigo Nodularis Presented (by invitation) by DR ROBERT C RANQUIST

Erythema Induratum and Papulonecrotic Tuberculid Presented by DR MICHAEL H EBERT and (by invitation) DR ALLEN S PEARL JR

A Case for Diagnosis (Leprosy?) Presented by DR EDWARD A OLIVER and DR SAMUEL M BLUEFARB

Lichen Planus with Atypical Microscopic Picture? Lichenoid Toxic Eruption Presented by DR STEPHEN ROTHMAN and (by invitation) DR R H SNAPP

Erythema Figurata Perstans or Tinea Superficialis Squamosa Presented (by invitation) by DR MAURICE OPPENHEIM and DR WILLIAM A YACULLO

Parapsoriasis en Plaques Limited to Flexural Areas Presented by DR EDWARD A OLIVER and Dermatology Staff

A Case for Diagnosis (Glossitis Rhombica Mediana of the Brocq-Pautrier Type?) Presented by DR JAMES R WEBSTER

A Case for Diagnosis (Parapsoriasis en Plaques? Premycotic Mycosis Fungoides?) Presented by DR RALPH H SCULL

A Case for Diagnosis (Pemphigus?) Presented by DR D V OMENS and (by invitation) DR HAROLD D OMENS and DR J GRAFFIN

Chronic Discoid Lupus Erythematosus—Persistent Despite Treatment for Thirty-Four Years Presented by DR JAMES R WEBSTER, DR SAMUEL BLUEFARB and (by invitation) DR J GRAFFIN

Scleroderma Presented by DR DAVID V OMENS and (by invitation) DR B YAFFE and DR HAROLD D OMENS

A Case for Diagnosis (Granuloma Telangiectaticum?) Presented by DR THEODORE CORNBLEET and (by invitation) DR H SCHORR and DR B YAFFE

Hodgkin's or lymphoblastoma type and the type described by Lewis, which seemed to be on an allergic basis and simulated changes seen in periarteritis nodosa In the case of eosinophilic granuloma of the bone reported by Curtis there were elevated granulomatous cutaneous lesions I saw a patient today with ulcerative lesions with decided changes in the bones of the skull which makes the disease in this case similar to Hand-Schuller-Christian's disease and Letterer-Siwe's disease My co-workers and I have observed a patient with multiple small granulomatous lesions with similar cystic lesions and rarefaction in the bones In another case in which our original diagnosis was histiocytoma, there were multiple small nodular lesions in the skin resembling xanthoma and bony lesions subsequently developed in the mandible Farber of Boston groups eosinophilic granuloma of the skin, Letterer-Siwe's disease and Hand-Schuller-Christian's disease together as variants of the same process and regards any evidence of deposition of fat in the tissue as a secondary degenerative phenomenon He therefore would differentiate these conditions from xanthomatosis and diseases of lipid metabolism Some years ago, however, Weidman reported a case of xanthoma disseminatum in association with Hand-Schuller-Christian's disease, and there are other such cases in the literature so that the exact classification of eosinophilic granuloma of the bone and skin remains to be determined

Noduloulcerative Syphilid of the Chest Wall Presented by Dr Herbert Rattner and (by invitation) Dr H Rodin and Dr N L Baker

Ulceronodular Syphilis of the Abdomen Presented by Dr James R Webster and (by invitation) Dr J Graffin

A Case for Diagnosis (Pyoderma Faciale?) Presented by Dr Theodore Cornbleet and (by invitation) Dr D Cohen and Dr J Graffin

Bromoderma, Granulomatous and Acneform Presented by Dr David V Omens and (by invitation) Dr Harold D Omens and Dr J Graffin

A Case for Diagnosis (Blastomycosis? Bromoderma?) Presented by Dr Francis E Senear and staff

Lymphangiectasis of the Vulva Presented by Dr Herbert Rattner and (by invitation) Dr H Rodin and Dr N L Baker

A Case for Diagnosis (Lichen Striatus? Nevus?) Presented by Dr Theodore Cornbleet

A Case for Diagnosis (Meleney's Ulcers or Pyoderma Gangrenosum?) Presented by Dr Theodore Cornbleet and (by invitation) Dr H Shorr and Dr N L Baker

Squamous Cell Epithelioma at the Site of Old Lupus Vulgaris Which Had Been Treated with Roentgen Rays Presented by Dr Theodore Cornbleet and (by invitation) Dr David Cohen

Pityriasis Lichenoides of Juliusberg Presented by Dr E A Oliver

A Case for Diagnosis (Mycosis Fungoides? Psoriasis?) Presented by DR JAMES R WEBSTER, DR SAMUEL BLUEFARB and (by invitation) DR N BAKER

Superficial Epithelioma on Sacral Area with Basal Epithelioma near the Anus Presented by DR THEODORE CORNBLEET and (by invitation) DR D COHEN and DR J GRAFFIN

A Case for Diagnosis (Acrodermatitis Chronicus Atrophicans) Presented by DR MICHAEL H EBERT and (by invitation) DR M S KAGEN

Nodular Leukemia Cutis in a 14 Month Old Boy, Duration Eight Months Presented by DR MICHAEL H EBERT and (by invitation) DR N L BAKER

Syringocystoma Presented by DR MICHAEL H EBERT and (by invitation) DR N BAKER

Francis W Lynch, M D, *President*

Leonard F Weber, M D, *Secretary*

June 18, 1947

Adenoma Sebaceum Presented by DR T CORNBLEET and (by invitation) DR H SCHORR and DR J GRAFFIN

R S, a Negro woman aged 23, as a child had frequent episodes of "spasms" which may have been epileptic-like in nature She finished the seventh grade in school at the age of 19 years, and she works as a dishwasher

On May 22, 1947, she entered a medical ward at Cook County Hospital with acute rheumatic fever Subsequently, she had a spontaneous pneumothorax, which is gradually disappearing

Examination reveals an eruption limited to the face which is predominantly on the central portion, chin and eyelids The lesions consist of dark brown papular nodules varying from a few millimeters to 1 cm Neurologic examination revealed no abnormalities Fundoscopic examination has not yet been completed

The Kahn reaction of the blood was negative Urinalysis showed albumin (1 plus) The examination of the blood showed hemoglobin 66 per cent, erythrocytes 3,530,000, leukocytes 5,600, with a normal differential count, and nonprotein nitrogen 22 mg per hundred cubic centimeters The sedimentation rate was 40 mm per hour

The roentgenogram of the chest originally showed a left total pneumothorax, at present there is a 30 per cent residue The roentgenogram of the ankles showed no abnormalities The histologic section from a nodule of the cheek is presented

DISCUSSION

DR M R CARO I agree with the diagnosis both clinically and histologically Histologic examination showed a fibromatous type of tumor rather than hyperplasia of sebaceous glands

DR ROBERT M B MACKENNA, London, England (by invitation) It was clearly shown in this case that the lesions are not present to any great degree

Parapsoriasis Guttata (Pityriasis Lichenoides Chronica) Presented by DR STEPHEN ROTHMAN and (by invitation) DR Z FELSHER and DR R SNAPP

Pityriasis Lichenoides Chronic Varioliformis Presented (by invitation) by DR MAURICE OPPENHEIM and DR W A YACULLO

Pityriasis Lichenoides et Varioliformis Acuta Presented by DR EDWARD A OLIVER and (by invitation) DR A B HENNINGSEN

Lupus Miliaris Disseminatus Faciei Presented by DR EDWARD A OLIVER and (by invitation) DR H F GARRARD

Sarcoidosis, Cutaneous Lesions of Boeck and Darier-Roussy Type Presented by DR FRANCIS E SENEAR and staff

A Case for Diagnosis (Acrodermatitis Atrophicans Chronica?). Presented by DR FRANCIS E SENEAR and staff

A Case for Diagnosis (Keratosis Pilaris?) Presented by DR M H EBERT and (by invitation) DR VERA LEAF

Pustular Psoriasis Presented by DR M R CARO, DR STEPHEN ROTHMAN and (by invitation) DR R SNAPP

Cicatrizing Alopecia Presented by DR DAVID V OMENS and (by invitation) DR HAROLD D OMENS

Leukemia Cutis Presented by DR FRANCIS E SENEAR

Francis W Lynch, M D, *President*

Leonard F Weber, M D, *Secretary*

May 21, 1947

A Case for Diagnosis (Erythrasma?). Presented by DR T CORNBLEET and (by invitation) DR H SCHORR and DR J GRAFFIN

Granuloma Inguinale Treated with Streptomycin Presented by DR M H EBERT and (by invitation) DR N BAKER

O N, a Negro aged 46, has been ill for fifteen years He has been a bed patient in the Cook County Hospital for the past twenty-eight months He was admitted in January 1945 with extensive ulceration of the inguinal areas, scrotum and perineum Smears of these areas showed Donovan bodies From July 1946 to February 1947 he was treated with podophyllum solution (20 per cent in liquid petrolatum) with some improvement On April 18 treatment with streptomycin was begun and given for one month, 120,000 units every three hours The process on the inguinal areas and scrotum has healed, on the perineum there is still a small ulcer (3 by 5 cm)

on the upper lid Epithelioma adenoides often attacks the upper lid, and adenoma sebaceum spares it

Contrast Sweating Above and Below Line of Paraplegia Presented by Dr T Cornbleet, Dr H Schorr and Dr N L Baker

H C, a Negro aged 25, was a patient at the Hines veterans' hospital from March 6, 1946 to January 1947 He complained of pain in the right leg and in the lower thoracic part of the spine, of four years' duration A laminectomy was done May 26, 1946, and a lesion was encountered at the level of the ninth thoracic vertebra which appeared to be an intramedullary cord tumor He was transferred to the Cook County Hospital Jan 20, 1947, where he complained of profuse sweating of the entire upper half of the body Injections of atropine sulfate afforded relief for two to three hours

Physical examination showed complete flaccid paralysis of the lower extremities Pain and pressure sense are diminished on the lower part of the abdomen and lower extremities There is no profuse sweating of the face, neck, upper extremities or trunk There are follicular keratoses of the sternum and other areas on the trunk

The urine contained albumin (1 plus) and many white blood cells The Kahn reaction of the blood was negative, and the blood cell count was normal The spinal fluid contained 330 cells per cubic millimeter, and the protein was 3,500 mg per hundred cubic centimeters

A roentgenogram taken after injection of opaque material indicated a complete block at the level of the ninth thoracic vertebra

DISCUSSION

Dr Stephen Rothman This is a good example of hyperhidrosis of organic central nervous system origin On the patient's back there are beginning signs of prickly heat, showing that softening of the horny layer and plugging of the pores occur in hyperhidrosis irrespective of whether it is peripheral or central in origin

Dr Theodore Cornbleet The patient presents all the changes in some areas that have been described for miliaria induced by heat Above the point of laminectomy and paraplegia there is excessive sweating, below there is excessive dryness The plugging of sweat pores and the changes that follow in miliaria are here reduplicated Thus it is excessive sweating itself which leads to cornification at the sweat duct orifices Heat is not necessary for the production of the syndrome, except in so far as it stimulates increased sweating

A Case for Diagnosis (Seborrheic Dermatitis) Presented by Dr Theodore Cornbleet and (by invitation) Dr D Cohen and Dr N L Baker

Cutaneous Blastomycosis, Therapeutic Result Presented by Dr F E Senear and staff

W S C, aged 57, was referred to the Department of Dermatology, Illinois Research and Educational Hospitals, in October 1946 with the diagnosis of blastomycosis, proved by biopsy Examination revealed an irregularly circinate plaque at the left commissure of the mouth, extending laterally on the cheek for about 8 cm The lesion was sharply marginated and had a precipitous border and a mammillated, somewhat elevated, crusted surface A few microabscesses were visible in the border, and the central portion of the lesion had healed, leaving a fine pinkish scar

DISCUSSION

DR ROBERT BARTON, Dubuque, Iowa (by invitation) Since 1946 at the Chicago Intensive Treatment Center 9 patients with granuloma inguinale have been treated with streptomycin In every case the lesions disappeared within forty-five days after treatment was instituted In 3 of the cases there have been relapses Streptomycin as my co-workers and I have used it may or may not cure granuloma inguinale, but to date it is the most effective drug for that disease The pattern in Dr Ebert's case conforms to that in ours After treatment was stopped the lesions continued to heal without additional therapy The patients returned perhaps a month or two later with the lesions completely gone It appears that once treatment is given, the effects are protracted

Werner's Syndrome (Progeria of Adults) Presented by DR T CORNBLEET and (by invitation) DR D COHEN and DR J GRAFFIN

Pigmented Purpuric Lichenoid Dermatitis Presented by DR T CORNBLEET and (by invitation) DR D COHEN and DR N L BAKER

T B, a white man aged 30, has had purplish spots on the legs and dorsum of the feet for two years These are asymptomatic In January 1945 the right testis and epididymis were removed because of tuberculosis

On both legs, mainly on the anterior aspect, there are lichenoid purpuric papules Similar lesions are present on the dorsa of the feet, in groups There are pigmented macules, 2 to 5 mm in diameter, among the papules of the legs and dorsa of the feet

Roentgenogram of the chest reveals a soft fuzzy infiltration in the right apex Biopsy by Dr Caro showed Gougerot-Bloom's disease

DISCUSSION

DR H E MICHELSON, Minneapolis Pautrier said that if we wish to advance dermatology, it would be well if we eliminated ten names a year instead of adding ten new ones Following his suggestion, I would like to eliminate the name Gougerot-Bloom's disease now Sooner or later, we must decide that all of these diseases that are characterized by localized hemosiderosis are one and the same thing and differ only in their extent and their localization Gracing them with long names is one of the troubles that dermatology has had to contend with for many years

Scrofuloderma, Pott's Disease and Retrosternal Abscess Presented by DR T CORNBLEET and (by invitation) DR H SCHORR and DR N L BAKER

A Case for Diagnosis (von Recklinghausen's Disease?) Presented by DR I M FELSHER, DR JULIUS E GINSBERG, DR A SLEPYAN and (by invitation) DR I EIRINBERG

Mrs L P, a well nourished, well developed, Negro woman aged 49, was first seen at Mandel Clinic, Michael Reese Hospital, on May 15, 1947 On the left buttock and left thigh there are present two large, well circumscribed tumors measuring 4 5 by 3 inches (11 by 7 cm) and 7 by 3 inches (18 by 7 cm), respectively These tumors have been present since birth but have caused the patient no difficulty with the exception of occasional discomfort when pressure is applied

Roentgen irradiation, in a total dose of 2,085 r, has been administered, along with potassium iodide orally in a maximum daily dose of 90 minims (about 6 cc) The lesion has cleared except for four small crusted areas at the periphery

Blastomycosis Presented by DR EDWARD A OLIVER and DR J M MCCUSKEY

The patient is a dairy operator and handles powdered milk The lesions appeared about four weeks ago

At present there are twelve nodular lesions on the face and the back of the neck, varying in size from that of a split pea to that of a hazelnut The lesions are erythematous, boggy and studded with pinpoint to pinhead-sized yellow pustules, especially at the periphery On the right hand, there is a deep, erythematous, indurated mass, the size of a hen's egg

Microscopic examination of material from the periphery of the lesions showed Blastomyces

DISCUSSION OF PREVIOUS TWO CASES

DR OLIVER S ORMSBY Years ago, when we had foreign guests, it was possible within a short period to bring in several patients with blastomycosis for demonstration Such cases are now comparatively rare There was a time when I had 100 cultures grown from 100 different patients Dr MacKenna can get no idea about what blastomycosis looks like by seeing the patients presented today One patient was cured with efficient treatment, and the other did not have typical lesions The skin lesions in a typical case are classic They occur in plaques with elevated margins and a superficial smooth scar in the center The margin of the lesion slopes and contains true abscesses in which Blastomyces are found The cases of systemic disease are different My co-workers and I had the privilege of reporting the first one in 1903, in which the lesions were clinically and symptomatically blastomycosis The lesions in that case consisted of subcutaneous abscesses, ulcerations and nodules We proved that the skin lesions came by way of the circulation At that time a large number of patients with systemic blastomycosis died—at least 50 per cent of the patients with systemic disease died The course was like that of severe pellagra some years ago I was in London when the disease was being discussed in this country, and the London men were much interested It was not until 1907, when many physicians from abroad were here to attend the international congress, that we were able to demonstrate to our foreign guests that blastomycosis was an entity—they thought it was syphilis I am sorry that Dr MacKenna did not see an example of the American variety of the disease

DR STEPHEN ROTHMAN We will have the opportunity to demonstrate a case of extensive American blastomycosis to Dr MacKenna tomorrow in Billings Hospital Dr Senear's patient has shown remarkable response to therapy In cases with widespread lesions the initial therapeutic effect of iodides is always impressive, but it takes years for them to clear up The lesions heal rapidly in the center but spread peripherally The supporting effect of local roentgen irradiations is rather modest Local application of fungicides is ineffective, in spite of their fair fungicidal action on Blastomyces in vitro We have not seen any beneficial effect of vaccine therapy Apparently cases with small simple lesions are easier to manage

DR. M J REUTER, Milwaukee In Dr Senear's case there is still some activity around the borders of the lesions In resistant plaques such as this, I

The tumors are extremely flaccid, lobulated and pendulous The skin covering them appears lighter and atrophic and at the periphery of the lesions is filled with giant comedos On palpation the lesions are firm and nodular

Microscopic sections taken from the edge and center of the lesion show hyperkeratosis, deep brown pigmentation of the basal layer, flattening of the rete processes and some hyperplastic sebaceous glands containing comedos The corium is replaced by a tumor mass of connective tissue cells containing many small blood vessels There are numerous mast cells present With the Van Gieson stain, the tumor tissue is essentially the same color as that of normal collagen The orcein stain shows absence of elastic fibers throughout the tumor



Lesions on the buttock and thigh of patient with diagnosis of von Recklinghausen's disease

Granuloma Fungoides, D'emblée Presented by DR THEODORE CORNBLEET

F S K, a white man aged 74, presents mushrooming tumors on the right wrist and posterior hair line Near the scalp lesion and on the left ear lobe there are several infiltrated plaques that are sharply outlined and of various sizes There is itching The lesions appeared eight months ago There were no preceding lesions of any kind or any itching The patient was in the hospital about the time of onset of the skin changes

Mycosis Fungoides Treated with Sodium Paraaminobenzoic Acid Presented by DR JAMES H MITCHELL

Mrs L McC, aged 52, was first seen on Jan 18, 1945, with a huge exuding tumor on the left ramus of the jaw There had been a generalized pruritic eruption for the past two years Various lesions of the type on the left cheek had appeared and had healed spontaneously with scarring

A clinical diagnosis of mycosis fungoides was made and confirmed by biopsy Intensive roentgen ray treatment was given to the point of tolerance on various occasions with good immediate response Intramuscular injections of chaulmestrol were begun on Jan 28, 1947, which were followed by an intense generalized toxic eruption

have been destroying the lesion with diathermy, at the same time giving the patient large doses of potassium iodide by mouth

DR THEODORE CORNBLEET The surgeons think that the dermatologists' approach to the treatment of cutaneous blastomycosis with medical measures is inadequate, inefficient and a loss of time They believe, at least some of them, that the lesions should be excised and the defects grafted They believe that even large areas are better treated with such a direct attack Their view is that as long as the disease is superficial breadth of area involved is a secondary consideration

DR FRED BECKER, Duluth, Minn Some investigators have expressed the belief that, prior to iodide therapy for systemic blastomycosis, a cutaneous test with a Blastomyces vaccine should be performed If the result is positive, it denotes allergy and desensitization must be performed, with gradually increasing doses of the vaccine until this positive cutaneous sensitivity is eliminated Then only should iodine therapy be instituted They cited several cases in which giving iodides produced rather disastrous results in a patient highly sensitive to the vaccine

DR STEPHEN ROTHMAN I understood that vaccine was required as initial therapy in cases with hypersensitivity to iodides and that the vaccine therapy was supposed to desensitize to iodides I wonder whether these observations have been corroborated In our case with no iodide sensitivity, vaccine therapy had no effect whatsoever although the patient shows strongly positive cutaneous reactions to the vaccine

DR ADOLPH ROSTENBERG JR (by invitation) I have had no firsthand experience treating blastomycosis As I understand Conant and his colleagues, a patient with systemic involvement who is allergic to a blastomycosis vaccine may have a spread of the blastomycosis if he is given iodides If the vaccine is given first some kind of immunity develops, so that the patient is subsequently able to take iodides The present immunologic point of view regarding diseases such as blastomycosis has altered considerably Primarily through the work of Dr Rich at Johns Hopkins Hospital it has been realized that there is dissociation between so-called immune phases and the hypersensitive phases of a disease and not, as originally stated, that hypersensitivity is a way station on the road to immunity This makes it questionable whether anything is accomplished from the point of view of immunity by desensitization in the tuberculin type of sensitization Possibly one succeeds only in abolishing or reducing the skin reaction

DR F E SENEAR Dr Ormsby recommended that arsphenamine therapy be employed when patients who had been receiving iodides for blastomycosis failed to show further progress and that after this procedure, with the use of but a few injections, the blastomycosis would again become responsive to iodide therapy

While I believe that American blastomycosis is not seen as frequently now as in the past, there has been a change in the clinical appearance of this disorder My co-workers and I have recently seen several patients with cutaneous manifestations from systemic blastomycosis, and in these instances a considerable number of widely scattered lesions have developed spontaneously About three years ago, I had, in the space of four months, 3 patients in this category The organism is readily demonstrable in lesions of this type We have also seen in recent years a larger number of patients with the deep-seated furunculoid, or cold abscess, type of lesion

At the suggestion of Dr Arthur Curtis, treatment with sodium paraaminobenzoic acid was begun March 29, tablets, 2 Gm, were taken every three hours during the waking hours The clinical improvement has been spectacular

DISCUSSION OF TWO PRECEDING CASES

DR HAMILTON MONTGOMERY, Rochester, Minn With respect to Dr Mitchell's case, the photograph of the patient shows a definite reaction apparently to chaulmestrol which I have been using for some time in cases of mycosis fungoides but with, on the whole, indifferent results There have been 1 or 2 cases in which striking improvement occurred Dermatitis from the use of chaulmestrol is an unusual occurrence

DR A C CURTIS, Ann Arbor, Mich Two months ago, at the meeting here, Dr Mitchell asked whether I could suggest anything that might be of value in his 2 cases of mycosis fungoides In both cases the roentgen response had been exhausted I suggested that he might try para-aminobenzoic acid Dr Zarafonetis, a member of our medical department, and I have been using sodium para-aminobenzoate in the treatment of some of the lymphoblastomas Because of its relation to the local anesthetics we thought that it might have some value in certain of the lymphoblastomas Our patients received 2 Gm of the sodium salt every two hours around the clock Dr Mitchell gave 2 Gm of the acid every three hours around the clock Some of our patients had a Herxheimer reaction characterized by redness and burning of the lesions The reaction would subside, and often the lesions would disappear The first patient we treated was something like the one Dr Mitchell showed today, a woman with a psoriasiform type of mycosis fungoides The effect of roentgen rays had long been exhausted She also improved rapidly on treatment The drug is by no means innocuous It has many disadvantages when given in large doses One is that it produces glycosuria, which seems to be related to a lowering of the renal threshold because the patient often has blood sugar values that are relatively low, 40 or 50 mg per hundred cubic centimeters In 1 patient with psoriasis hypoglycemia of such severity occurred that treatment with the drug had to be stopped Some patients have nausea and some fatigue In 1 case we had to stop use of the drug because of the Herxheimer-like effect How it acts and whether its reaction will be sustained have not been determined

DR H E MICHELSON, Minneapolis My co-workers and I have tried urethane in Kaposi's sarcoma with no effect We did have some effect with nitrogen mustard We also had temporary results with nitrogen mustard in mycosis fungoides

DR STEPHEN ROTHMAN It was interesting to note in this case that, while the premycotic lesions were highly pruritic, the tumors themselves do not itch In my experience this is the rule Pruritus is present as long as there is a defense reaction of the skin against the deposition of foreign cells After the infiltrating tumor has established itself and started unlimited growth, itching subsides

The experience with nitrogen mustards in Billings Hospital has been that about in 50 per cent of the cases of Hodgkin's disease the cutaneous manifestations react favorably The practical significance of this therapy is that it is effective in cases in which the beneficial effect of roentgen rays has been exhausted However, the final outcome has not been changed so far

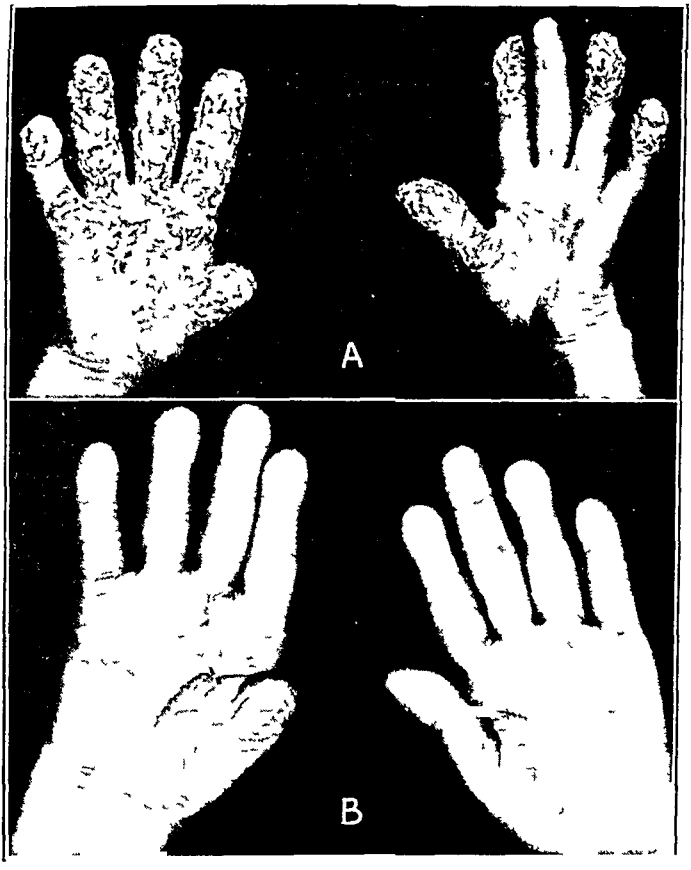
DR EDWARD A OLIVER With reference to Dr Cornbleet's patient, I have watched the man for the last seven years He has been a constant attendant in our clinic at Northwestern University, and we have always presented the case as

Kaposi's Sarcoma Presented by DR JAMES H MITCHELL, DR RALPH SCULL and (by invitation) DR B YAFFE

Hidrosadenitis Suppurativa, Acne Vulgaris and Acne Conglobata, DR E E SENFAR and staff

Pustular Psoriasis, Healed After Tobacco Juice Soaks Presented by DR STEPHEN ROTHMAN and (by invitation) DR J H MCCREARY

S J, a housewife aged 57, was presented at the Chicago Dermatological Society meeting of Oct 16, 1946 The diagnoses suggested were pustular



Pustular psoriasis treated with tobacco juice soaks *A*, before treatment *B*, after treatment

psoriasis and acrodermatitis continua She had been hospitalized at the Albert Merritt Billings Hospital from June 12 to October 22 for observation and treatment

The patient was discharged from the hospital, unimproved, one week after the presentation, to be followed as an outpatient While at home, on her own initiative, she soaked her hands in hot tobacco juice six to eight times a day The juice was prepared by boiling tobacco in water for two minutes Each soaking lasted five to ten minutes Within one week considerable improvement

one of psoriasis of the plaque type Itching is present, but I have seen Negroes with psoriasis who do have considerable pruritus He gets worse and gets better I examined the slides, and I do not believe that one could make a diagnosis of mycosis fungoides from them

DR ADOLPH ROSTENBERG (by invitation) What percentage of cases of parapsoriasis en plaque become cases of mycosis fungoides?

DR HAMILTON MONTGOMERY, Rochester, Minn In a fairly large series of cases that I studied with Burkhart (ARCH DERMAT & SYPH **46**.673-690, [Nov] 1942), we came to the conclusion that parapsoriasis remains as such and does not eventuate in mycosis fungoides Mycosis fungoides may start out looking like parapsoriasis and remain as such for many years, but when the cases are studied in the early parapsoriatic-like stage histologic changes of mycosis fungoides are already demonstrable, including clumping of cells, pyknosis, karyorrhexis and multiplicity of cell types in the infiltrate Dr Sweitzer and his associates have presented a case of supposed parapsoriasis many times in the course of the last fifteen years Dr Madden obtained numerous specimens of biopsy from the beginning, about fifteen in number Two thirds of these biopsy specimens revealed definite features of mycosis fungoides, and I anticipate that this patient eventually will have all the clinical features of that disorder

DR S W BECKER I distinctly remember the late Professor Bloch saying that Brocq had abandoned the term erythrodermie pityriasique en plaque disseminée He said that he no longer held to the belief that there was a type of parapsoriasis to which he gave this name

DR OTTO H FOERSTER, Milwaukee There now are perhaps about a dozen undisputed cases of parakeratosis variegata on record The disease in several of the original cases, when seen again at a later time by Unna, was found to have undergone a clinical change and was recognized by him as mycosis fungoides

DR THEODORE CORNBLEET The initial lesion that my patient showed was a well developed tumor, which classified his disease as the d'emblee variety Subsequently there was regression to the second, or infiltrative, stage with extensive lesions Thus various stages may be present simultaneously, and their mode of evolvement and progression may follow different patterns A patient at the Cook County Hospital was treated recently with the relatively new nitrogen mustard method In a disease with a course as capricious as mycosis fungoides it is difficult to be sure, but this form of therapy seemed to have hastened this particular patient's death An autopsy was made, and the heart, liver and other viscera were found to have heavy infiltrates with characteristics of granuloma fungoides Some of the newer fission products may improve the prognosis in the lymphoblastomas, though thus far they have not done what could not be achieved with the older radiation modalities

Sarcoidosis. Presented by DR S ROTHMAN and (by invitation) DR E L LADEN

M H, a Negro woman aged 31, is a seamstress whose illness began in 1942 with a nodular lesion on her left upper arm This increased in size, and new lesions appeared on her face, right arm and left leg in the intervening years

In 1943 she suffered from short-lasting attacks of pain in the left ankle and knee This disappeared spontaneously after ten months In November 1946, she noted swelling of the proximal phalanx of the third finger, right hand This has become progressively worse

The patient was seen by the Chest Department of the University of Chicago Clinics in February 1945 Results of tuberculin skin tests with dilutions of

was seen in all the treated lesions, and almost complete cure of the hands and fingers was achieved in four weeks

Dr Edward Laden of our department could not demonstrate any antibiotic effect of the tobacco juice in vitro

Dermatitis Repens, Therapeutic Result Presented by DR F E SENEAR and staff

E L, aged 63, has been a patient on the dermatology service, Illinois Research and Education Hospital, since October 1946, with the diagnosis of dermatitis repens, affecting the first and second toes of the right foot On a previous admission intractable pain associated with a similar eruption on the left foot had necessitated amputation up to the middle of the thigh During the present period of hospitalization the following therapeutic agents were tried without noticeable improvement penicillin parenterally in large doses, sulfonamide drugs, staphylococcic toxoid, wet dressings of silver nitrate potassium permanganate and benzalkonium chloride, tyrothricin dressings, streptomycin ointment and repeated lumbar sympathetic blocks The most recent treatment has included a course of sulfapyridine by mouth and roentgen irradiation (twelve doses of 50 r, given twice weekly, terminating on May 12, 1947) No improvement was noted Immediately after application of compound tincture of benzoin ointment was started (May 28), oozing and crusting disappeared and epithelization began At present there is only a small area of dry healing granulations at the tip of the great toe

Pustular Psoriasis, Treated with Tobacco Juice Soaks Presented by DR STEPHEN ROTHMAN and (by invitation) DR J C MCCREARY

M K, a white housewife aged 53, was admitted to Albert Merritt Billings Hospital May 18, 1947, presenting widespread psoriasis of forty-eight years' duration Approximately fifteen years ago the palm of the right hand became pruritic and then pustular Some of the joints of the hand stiffened Later the tips of the fingers and toes became red, swollen and full of pustules Some nails were shed Repeated cultures failed to grow bacteria There have been remissions with improvement, of several years' duration, but never complete healing The present flare-up began four months prior to admission

In the past, various methods of therapy had been tried, including local applications of tyrothricin, penicillin, nitrofurazone, chloresium, ammoniated mercury, tar, roentgen irradiations, systemic administration of arsenic and vitamin B complex and a fat-free diet

Examination revealed well circumscribed, erythematous, partly crusted and partly hyperkeratotic patches on the scalp, trunk and upper and lower extremities The hands and toes showed subcorneal pustulation and crusting The right hand showed atrophy and contractures Both hands had stiffened interphalangeal joints Some finger nails and toe nails were missing, others were rudimentary

Wassermann and Kahn reactions of the blood were negative The urine was normal Examination of the blood revealed 12,800 leukocytes The differential count was normal Hemoglobin was 12 8 Gm Erythrocyte cells numbered 3,370,000 Blood lipids and cholesterol were normal The results of the sternal bone marrow examination was normal The basal metabolic rate was + 2 per cent A roentgenogram of the hands showed moderate arthritic changes involving the interphalangeal joints The electrocardiogram showed a tendency to left axis deviation

1 1,000, 1 100 and 1 10 and undiluted tuberculin were all negative A roentgenogram of the chest showed moderate enlargement of the hilar lymph glands bilaterally Results of laboratory studies in 1945, including urinalysis, complete blood cell count, serologic reactions, and serum protein, were all essentially normal No skeletal lesions were found in 1945

The patient was seen in the Dermatology Clinic on May 13, 1947 Examination revealed multiple nodules and plaques on the face, extensor aspects of the arms and the left leg These lesions are firm and elastic to touch Many of the face lesions are depigmented The plaquelike lesions show a tendency toward central involution with a spreading border The lesions are dull brown to purplish Enlargement of the proximal phalanx of the third finger of the right hand was noted A roentgenogram of the hand showed widening of the base of this phalanx The medullary spaces are widened with intervening thin trabeculae The cortex is intact.

Treatment with vitamin D_2 (drisdol®), 150,000 units daily, was started on May 13, 1947 On May 16 she noted a flare-up of the cutaneous lesions with subjective throbbing sensations When seen on May 20, the flare-up had partially subsided, but some swelling was still noticeable

A biopsy specimen of a cutaneous lesion showed mild acanthosis of the epidermis The dermis contains a dense infiltrate consisting of lymphocytes, epithelioid cells and a few polymorphonuclear leukocytes In the deeper part of the corium there are well defined nests of infiltrate surrounded by connective tissue Vascular dilatation and some connective tissue degeneration are present

DISCUSSION

DR H E MICHELSON, Minneapolis I think that Negro patients having what is known as sarcoidosis should be observed in a most thorough manner to determine whether this uniform condition as seen in Negroes is the same as sarcoidosis in white persons, which might enable one to find out whether sarcoidosis is or becomes tuberculosis I have tried vitamin D_2 in 5 patients, with the dosage used in lupus vulgaris, and have seen no appreciable results

DR ARTHUR C CURTIS, Ann Arbor, Mich Although sarcoid is a clinical entity, I do not think that it is an etiologic one, unless one wishes to consider that perhaps a chemical compound is its cause This may be illustrated in the work originally done by Florence Sabin, when she began her work on fractionation of the tubercle bacilli She injected each fraction into animals, and sarcoid lesions developed in those receiving the phosphatide Further work has been done by others The late Dr Gardner, of Saranac Lake, insufflated animal lungs with silica dioxide and obtained typical sarcoid lesions Later Dr Allon in Toronto repeated Gardner's work and obtained the same results but noted considerable fat in the sections He then extracted these lungs with a solvent, removed the silica and reinjected the silica-free material into animals and again obtained sarcoid-like lesions This work indicates that silica may be an etiologic factor in sarcoid, silica produces the phosphatide which Sabin showed to be the chemical substance capable of producing sarcoid in animals

Not long ago a young man was seen with a typical sarcoid lesion of the face, proved by biopsy Dr Weller saw a few particles of silica in this lesion The next time I saw the patient I learned that two years previously he had been in an automobile accident and thrown out of his car, abrading his cheek on a gravel road I think that his sarcoid was due to silica ground into his cheek by the accident

Dr Michelson said that he has used vitamin D_2 without success That is not my experience The patients my co-workers and I have selected have had extensive

Biopsy of left knee joint capsule showed no abnormalities Biopsy of the skin showed changes typical of pustular psoriasis

While the patient was in the hospital, fever therapy was employed four times, with typhoid vaccine given intravenously (each reading 102 F) with no effect On June 4 the patient started soaking one finger in hot tobacco juice Within three days the swelling had gone and the finger had so improved that the patient was encouraged to soak the right hand Treatment has been continued in the following manner The tobacco is boiled for two minutes in water The hands are soaked in the heated extract for thirty minutes, four to six times a day The solution should be as warm as the patient can tolerate without burning

DISCUSSION

DR S W BECKER I think that the disease in all these patients is of the acrodermatitis continue type rather than the pustular psoriasis type The woman with the lesion on the arm shows a definite atrophy following healing, which rules out psoriasis The results from the bizarre treatment are certainly remarkable

DR F E SENEAR We have had this subject up here so often that nearly everything is repetitious I would like to agree with Dr Becker that the disease in these cases, at least the cases of extensive disease, is of the acrodermatitis continue type rather than pustular psoriasis I think that anyone would point out these lesions on the forearm as being a point against acrodermatitis continue, but the lesions on the tips of the fingers with the extensive undermining of the periphery are suggestive of the Hallopeau type

DR ROBERT M B MACKENNA, London, England (by invitation) I agree with everything Dr Senear has said Most of my colleagues would regard these as acrodermatitis continue type of lesions and not pustular dermatitis

DR STEPHEN ROTHMAN The patient started this treatment on her own She heard about it from neighbors The tobacco is boiled for two minutes only Our main purpose in showing these patients was to ask the members of this society to send more patients to us for testing the efficacy of this method with fractions of the tobacco juice in order to isolate the active compounds Of course, we shall need a number of patients with pustular psoriasis and with acrodermatitis Hallopeau to carry out this work

Lupus Vulgaris Improved with Vitamin D_2 Presented by DR F E SENEAR and staff

Lupus Miliaris Disseminata Facei, Improvement from Treatment with Vitamin D_2 Presented by DR HAROLD SHELLOW

Fox-Fordyce Disease, Relief with Testosterone Presented by DR F E SENEAR and staff

Congenital Syphilis, Second and Third Generation Presented by DR JAMES H MITCHELL and DR RALPH SCULL

Lipomelanotic Reticulosis (Pautrier-Woringer Disease) Presented by DR STEPHEN ROTMAN and (by invitation) DR M J SCHERBER and DR E L LADEN

R L, aged 63, was admitted to St Joseph Hospital in Chicago on April 30, 1947, with the complaints of swelling, redness and weeping of the skin of the

the pedigree of a family in which some members had psoriasis, others arthritis and one member arthropathic psoriasis The peculiar observations of the biopsy of the joints will be reported by our orthopedic department In 1 case the verrucous lesions developed the second time around healing psoriatic lesions

Eosinophilic Granuloma Presented by DR EDWARD A OLIVER and (by invitation) DR E LORANT

M E C, a white man aged 42, first noticed a few reddish lesions on his face in January 1943 The lesions developed slowly, and the patient was kept under observation in a Naval dispensary A biopsy was performed in September 1943 and another in March 1944 On both occasions the diagnosis on pathologic examination was "chronic inflammation, probably mycosis fungoides"

From October to December 1943, he had eight roentgen irradiations at weekly intervals, of 75 r each After completion of the irradiations the lesions flattened and changed color from cherry red to pinkish brown However, three months after the roentgen therapy was completed the lesions became active again and have shown occasional activity to date

The patient now shows a quarter-sized lesion on the left cheek, another irregularly shaped quarter-sized lesion on the right cheek and a larger lesion in front of the right ear on the temporal region These lesions are nonelevated and reddish brown and are yellowish brown on pressure with a diascope They are not pruritic

The general physical examination and roentgenograms of the chest, feet and hands showed no evidence of pathologic changes

The urine was normal Examination of the blood showed a hemoglobin content of 87 to 90 per cent, a color index of 0 9, an erythrocyte count of 4,500,000 to 4,600,000 and a leukocyte count of 6,000 to 9,600, with a differential count of 48 to 56 per cent neutrophils, 38 to 46 per cent lymphocytes and 6 per cent eosinophils The sedimentation rate was 2 to 4 mm per hour The total protein was 6 9 mg per hundred cubic centimeters of blood, with an albumin-globulin ratio of 1 7 to 1

In a recent biopsy histologic observations were as follows The epidermis was uniform and apparently not increased in thickness There was slight hyperkeratosis The basal cells were well preserved, with a small amount of pigment present

In the corium completely separated from the epidermis there were large and small clusters of cells as well as cellular infiltrations composed of numerous lymphocytes, an occasional eosinophil, a few plasma cells and a few neutrophils were seen also The blood vessels and lymphatics were slightly dilated and presented occasional perivascular infiltrate There was slight edema throughout the corium The sebaceous and sweat glands were not especially involved

Histologic examination showed the epidermis to be normal In the middle portion of the corium, separated from the epidermis by a narrow band of normal connective tissue, lay a wide horizontal band of cellular infiltrate This cellular mass was densely packed, it was sharply circumscribed, and it included within its borders hairs and sebaceous glands There were many eosinophilic polymorphonuclear and mononuclear cells and many lymphocytes and histiocytes and fewer plasma cells

DISCUSSION

DR H M BULEY, Champaign, Ill During the past eighteen months my co-workers and I have had the opportunity to see several cases of eosinophilic granuloma of the skin representing various types of eruptions As has been stated in previous discussions, it is extremely difficult to find the common denominator for the various pictures presented in these cases I feel, therefore, that it is some-

what premature to suggest common causative factors, at least not until a larger number of case studies have been accumulated The case presented today is comparable to the case described by Pasini in 1940, and also with the case I presented here in November 1945 In these 3 patients the eruption started with macular erythema on the face, which within several months changed to a more or less extensive papular or nodular form Once the lesions reached their maximum size, however, they maintained their clinical appearance It is further remarkable that the disease did not interfere with the patients' general health No pathologic changes were found in either the lungs or the bones Although there was a slight increase in the eosinophil count of the blood the disease was essentially confined to the skin In all 3 cases the lesions were indolent, causing no discomfort to the patient In the patient presented today, relative lymphocytosis (30 to 40 per cent) was found, which, as far as I can recall, had not been noted in the other cases

DR CARL W LAYMON, Minneapolis There have been less than a dozen cases of eosinophilic granuloma of the skin in the literature, and the association of eosinophilic granuloma of the skin and bone is extremely rare The clinical picture of eosinophilic granuloma of the skin is subject to wide variations The lesions may be papules, nodules or plaques which are smooth or verrucous and usually red, purple or brown In the case recently reported by Dr Lewis and Dr Cormia there seemed to be an association between the eosinophilic granuloma and a fungous infection of the feet These observers suggestd that possibly eosinophilic grauloma of the skin might be linked to allergy of infection

DR EDWARD A OLIVER In this case the disease was difficult to diagnose clinically The patient stated that he had been treated in the Navy for mycosis fungoides He had received eight roentgen treatments I knew that it was not mycosis fungoides, and my first impression was that it was sarcoid Dr Caro then examined the sections for me, and his diagnosis was eosinophilic granuloma Dr Buley recently published an excellent article on eosinophilic granuloma in the December 1946 issue of the *Journal of Investigative Dermatology* This disease is most difficult to diagnose clinically because it occurs in so many different forms Only by a careful study of microscopic sections can one be sure of the diagnosis

Urticaria Pigmentosa of Recent Origin in an Adult, with No Mast Cells in the Section Presented by DR S J ZAKON and (by invitation) DR A L GOLDBERG

A Case of Urticaria Pigmentosa in a Child, with Mast Cells in the Corium. Presented by DR E A OLIVER and (by invitation) DR H F GARRARD

Preauricular Sinus Congenita (Bilateral) Presented by DR CLEVELAND J WHITE

Hyperplasia of the Gums Due to the Use of Dilantin® Sodium (Diphenylhydantoin Sodium) Presented by DR E M SMITH JR

DISCUSSION

DR ADOLPH ROSTENBERG JR (by invitation) Dilantin® is chemically closely related to the German drug nirvanol (phenylethylhydantoin) Van Wyk and Hoffmann (Periarteritis Nodosa, *Arch Int Med* **81** 605, 1948) pointed out the paucity of reactions seen with dilantin® and the large number seen with nirvanol, which is interesting considering the extremely close chemical relationship

entire body of one year's duration This ailment started with a pruritic dermatitis on the ankles and elbows, which the patient attributed to contact with brick and lime dust In a few months it had spread to involve the entire body He was treated with local applications and injections with only temporary relief During the first six months of the illness the patient lost 26 pounds (12 Kg) in weight

In March 1947, the patient suffered an acute abdominal episode, which was interpreted as thrombophlebitis of the mesenteric veins, followed by generalized peritonitis

On admission to the hospital in April, there was diffuse erythema, swelling and oozing of most of the body The face and large flexures displayed lichenification Pruritus was intense There was generalized lymphadenopathy with single, hard, enlarged lymph nodes The tongue was beefy red and infiltrated, grayish plaques were present between the soft and hard palate The patient was afebrile

The acute manifestations of the dermatitis were checked by local applications When the patient was seen by the consulting dermatologist at this time the impression was erythroderma due to some lymphoblastomas

Laboratory examinations revealed negative serologic reactions, normal urine, erythrocytes 4,000,000, hemoglobin 10 5 Gm and leukocytes 21,000, with 69 per cent polymorphonuclear cells, 13 per cent lymphocytes, 9 per cent eosinophils, 2 per cent monocytes, 1 per cent basophils and 6 per cent stab cells Plasma proteins were 6 5 Gm per hundred cubic centimeters, albumin 2 8 Gm and globulin 3 7 Gm per hundred cubic centimeters with a ratio of 1 1 3 Sternal puncture showed hyperplasia of neutrophil precursors and a decrease in percentage of erythroblasts The left shift of neutrophil precursors was not pronounced enough to permit a diagnosis of myelogenous leukemia It was thought to be a leukemoid reaction Biopsy of the skin and lymph node was performed The microscopic skin sections showed chronic inflammation with a great number of melanophores and large pale cells with vesicular nuclei In the lymph node specimen the cortex is infiltrated by large pale cells, eosinophils, numerous pigmented cells and some polymorphonuclear and plasma cells

During his hospital stay the patient had two attacks of septic thrombophlebitis with positive blood cultures of hemolytic Staphylococcus albus, each time recovering after penicillin and dicumarol® therapy

The pruritus was greatly relieved by roentgen irradiations Several blood transfusions were given

During the observation period there has been a conspicuous darkening of the skin leading to the now prevailing color shade The leukocyte count has varied between 10,000 and 25,000 The relative lymphocytopenia has become progressively worse, down to 6 per cent lymphocytes with 88 per cent polymorphonuclear cells and a leukocyte count of 17,200

DISCUSSION

DR HAMILTON MONTGOMERY, Rochester, Minn I wonder whether a new name is needed or whether this should be called a new disease One sees deposition of melanin pigment in the lymph nodes in a great many inflammatory conditions, in association with lymphoblastomas, in psoriasis and also in conditions in which there is excess pigment in the skin In the case presented today the second biopsy simply revealed a nonspecific dermatitis, in other words, this man had an exfoliative dermatitis or generalized erythroderma without evidence of lymphoblastoma There is increased pigment in both the skin and the lymph nodes

DR ADOLPH ROSTENBERG JR (by invitation) As I understand this term, it does not really designate a cutaneous diagnosis It is purely a pathologic term

DR W R HUBLER I do not believe that she has pemphigus There are numerous, annular, bullous lesions on the face and shoulders The symmetric distribution of the eruption and the localization on the neck, axillas, elbows, knees and shoulders, as well as the grouping of the lesions, all point to a herpetiform type of eruption The patient is Rh negative, the husband Rh positive, and she is beginning to have anti-Rh antibodies About six months ago she was hospitalized by a gynecologist for what was apparently an early spontaneous abortion This would account for the early rise in anti-Rh titer I do not know what the Rh titer has to do with herpes gestationis, but I feel that some factor might be implicated since it usually clears with termination of pregnancy Therapeutic abortion should be performed in this case, because in a number of cases in which the patients were allowed to go to term, the percentage of monstrosities among living children was much higher than normal and stillbirths were common (Mueller, C *Am J Obst & Gynec* **48** 170-180 [Aug] 1944) Also, in some cases the herpetiform eruption persists after the completion of pregnancy when the patient is allowed to go to full term

NOTE—The follow-up examination of August 1947 showed that the eruption had subsided strikingly after a therapeutic abortion However, punctate, small vesicles persist in the groin and axillas, on the chin and in other scattered areas These are subsiding with inorganic arsenical therapy Hyperpigmentation has developed further showing the relationship to dermatitis herpetiformis The anti-Rh titer, three months after the therapeutic abortion, is only 1 1

Extensive Circumscribed Myxedema Presented by DR M J GIBANS, Akron, Ohio

H O , aged 56, was subjected to a subtotal thyroidectomy in February 1945 because of a toxic goiter Preoperatively the basal metabolic rate varied from + 72 to + 79 per cent, and the blood pressure was 154 systolic and 84 diastolic Postoperative examinations showed metabolic rates of + 27 and + 40 per cent, and finally — 15 per cent, and the blood pressure was 130 systolic and 70 diastolic His weight, which had been 130 pounds (59 Kg) before operation, increased to 179 pounds (81 Kg) thereafter About four months after operation, the patient noticed a little discoloration and redness about the ankles This progressed slowly until some months later, after he had returned to work, when it extended rapidly This has never caused him any discomfort

He now has nonpitting, tawny, elevated, nodular plaques, with moderately enlarged follicular openings, on the anterior aspects of both legs These plaques are much more extensive on the right leg, involving almost the entire lower half and extending over the medial surface and posteriorly, where there is one unusually large and firm mass, about 2 inches (5 cm) in diameter

The microscopic description by Dr Lloyd Catron was as follows There are slightly increased deposits of melanin in the epidermis, with edema of the corium The hair follicles are dilated and plugged with keratohyaline material The small blood vessels are thick walled There is a patchy infiltrate, composed chiefly of lymphocytes, around accessory skin structures The histologic appearances are compatible with circumscribed myxedema The patient has recently been given thyroid extract, 2 grains (130 mg) daily

Bullous Eruption (Pemphigus) Presented by DR E GILLESPIE, Canton, Ohio

Dermatitis Herpetiformis (?) in a Seven Year Old Girl Presented by DR H A HAYNES JR

Hurwitt (*J Invest Dermat* **5** 197 [Aug] 1942) reviewed all the lymph nodes taken out at the Mount Sinai Hospital, New York There is a reticulum and histiocytic cell replacement of the lymphocyte in the lymph node It is purely a benign process and is not related to lymphoblastoma Hurwitt also criticized the term Pautrier-Woringer disease and used the name dermatopathic lymphadenitis About a year later there was an article by Larkin and his co-workers (*J Pediat* **24** 442 [April] 1944) on this same syndrome, with reference particularly to infantile eczema He pointed out that involvement of the lymph nodes is not uncommon in infantile eczema and that these nodes can have a resemblance to those seen in Hodgkin's disease He warned against confusion with manifestations in Hodgkin's disease because this condition is benign

DR S W BECKER I have been of the opinion that this reaction was of a nonspecific variety Someone, some months ago, said that the pathologist at Cook County Hospital considered it a definite entity

DR S M BLUEFARB The original article on lipomelanotic reticulosis was written by Pautrier and Woringer in 1932 (*Bull Soc franç dermat et syph* **39** 947, 1932) They described 6 cases in which the three cardinal signs were exfoliative dermatitis, superficial generalized lymphadenopthy and pigmentation of the skin At that time no specific causative factor was mentioned In a second communication in 1940 Pautrier and Woringer described a case of generalized erythroderma in which typical lesions of mycosis fungoides developed and in which the original lymph node biopsy showed the appearance of lipomelanot c reticulosis and a subsequent one a reticulum cell proliferation found in mycosis fungoides They suggested that there might be a causal relationship between the two conditions At the February 1945 meeting Dr Oliver (ARCH DERMAT & SYPH **54** 621 [Nov] 1946) showed a case of generalized erythroderma with lipomelanotic reticulosis Several months later the patient died of mycosis fungoides

There appear to be several schools of thought regarding the outcome of this disease Dr Rostenberg just mentioned the benignity of this disease I believe that Robb-Smith of England also favors the concept of a benign condition as the patients in the 3 fatal cases in his series appeared to die from intercurrent disease rather than from the skin condition (*Brit J Dermat* **56** 107 [May-June] 1944) However, I do not believe that the disease in all these cases can be considered benign and that one should give a guarded prognosis because in a certain percentage of these cases one of the lymphoblastomas will develop

DR STEPHEN ROTHMAN I share the skeptic attitude of Dr Montgomery concerning the assumption that this is a separate entity On the other hand, the microscopic picture of the lymph nodes is not one of banal chronic inflammation, because the infiltration is invasive, neither does the picture correspond with that of any of the known lymphoblastomas When first seen, this patient had erythroderma with lichenification

Mycosis Fungoides Treated with Sodium Paraaminobenzoic Acid Presented by DR JAMES H MITCHELL

Mrs L McC, aged 52, was presented at the meeting of May 21 At the suggestion of Dr Arthur Curtis, treatment with sodium paraaminobenzoic acid was begun March 29, 1947 Tablets of 2 Gm were taken every three hours during the waking hours The clinical improvement was at first spectacular, but there has been little change in her condition in the past month

Circumscribed Scleroderma Presented by DR F M MCDONALD, Akron, Ahio

Lichen Striatus Involving the Leg of a Four Year Old Girl Presented by DR F M MCDONALD, Akron, Ohio

Porokeratosis of Mibelli Presented by DR C L BASKIN, Akron, Ohio

T N, a 70 year old man, a native of Italy, came to the United States forty-five years ago His inability to understand the English language prevents a complete history in this case His general health has always been good, he has never lost time from work

The present eruption began when he was a small child, gradually spreading from a spot on the left calf to include the entire leg and a large area of the sole The lesions show the characteristic threadlike border and polycyclic configuration There has been a slow steady advance of the margins during these many years All laboratory examinations showed normal values

DISCUSSION

DR G W BINKLEY This is a giant form of porokeratosis of Mibelli In addition to the appearance of the lesion, the long duration and the patient's Italian nationality are points in favor of a diagnosis of porokeratosis of Mibelli There is a sharp border between the normal skin and the involved skin

DR. W R HUBLER I believe that vitamin A has been used in the treatment of porokeratosis of Mibelli with some success At the last meeting of the American Academy of Dermatology a patient with this disease was presented, and several dermatologists stated that they had noted improvement following administration of large doses of vitamin A

George W Binkley, M D, *President*
D N MacVicar, M D, *Secretary*
Sept 25, 1947

Acrosclerosis with Calcinosis Presented by DR CHARLES MARTIN JR (by invitation)

Poikiloderma Atrophicans Vasculare with Changes of Mycosis Fungoides, Basal Cell and Squamous Cell Epithelioma Presented by DR W MARMELZAT and DR A E WALKER (service of DR H N COLE and DR J R DRIVER)

A Case for Diagnosis (Parapsoriasis? Erythrodermie Congénitale Ichthyosiforme?) Presented by DR E W NETHERTON

A Case for Diagnosis (Tuberculosis Cutis?) Presented by DR G H CURTIS and DR E W NETHERTON

Steatocystoma Multiplex (Pringle) Presented by DR H N COLE and DR J R DRIVER

Epidermolysis Bullosa Presented by DR JOHN BONNER for DR C F MCKHANN (by invitation)

DISCUSSION

DR JAMES H MITCHELL The patient was shown last month, and I asked her to come here especially for examination by Dr MacKenna I might say that since she was last presented she has made less progress than she made previously Dr Ormsby pointed out that many different medicaments could improve mycosis fungoides temporarily, and perhaps this medicament will fit in with what Dr Ormsby has said I have another patient treated by the same method and a third one with leukemia It remains to be seen whether we have anything worth while

NOTE—The patient with lymphatic leukemia died without making a satisfactory trial of the medicament The other 2 patients are still doing well

A Case for Diagnosis (Alopecia Areata? Atrophic Glossitis? Acquired Anhidrosis?) Presented by DR FRANCIS W LYNCH

Miss G L, aged 24, first had a dermatologic condition at the age of 14, when she had a febrile illness, possibly rheumatic fever, followed by a generalized eruption which was first regarded as scarlet fever The eruption recurred three times, accompanied with fever and followed by exfoliation After the last febrile attack the exfoliation continued, accompanied with pyogenic infection especially on the hands, feet and scalp, resulting in loss of the nails and alopecia There was also otitis, conjunctivitis and gingivitis About that time the skin on the chest and abdomen became inflamed and was wiped off easily, leaving a moist red surface which subsequently healed The patient was bedridden seven months She lost 67 pounds (30 Kg) in weight

Subsequently there has been persistent alopecia which is almost total There is photophobia and a severe refractile error There was amenorrhea for one year, but the menses again became normal During hot weather she perspires slightly and becomes weak, and her temperature rises to 103 F or more

The family history is normal except that one sister had eczema in infancy The patient has had occasional urticaria

The scalp is almost bald, with some occipital hair remaining There are a few hairs in the lashes and brows, the body and extremities are without hair The bulbar conjunctivas are slightly red and the palpebral conjunctivas show some pale areas and other inflamed areas (They previously were treated by electrosurgery) The tongue presents superficial atrophy The left buccal mucous membrane shows an irregular area of thickening and possibly scarring All the nails are atrophic and deformed The palms and soles are dry and appear to be scarred The extremities are smooth and hairless, and the skin of the legs is thin There are numerous irregular brown macules on the face and hands

DISCUSSION

DR S W BECKER This is an odd case It started out at the age of 14 when the patient had a severe febrile reaction, during which she lost her hair I suppose it was on a systemic basis Later she had a recurrence of the generalized eruption, which she said looked like scarlet fever It recurred a great many times She had a severe crusting eruption of the scalp She obviously has a certain amount of cutaneous scarring, which I presume resulted from the inflammatory reaction She lost not only her hair but her finger nails as well Her tongue is somewhat atrophic, and I thought that there was a little leukoplakia on the tongue and buccal mucosa The palms and soles were peculiar in that she had fungated keratoses which were a little suggestive of an arsenical keratosis I questioned

Acrodermatitis Chronica Atrophicans Presented by DR A E WALKER and DR W MARMELZAT (service of DR H N COLE and DR J R DRIVER)

Scleredema Adultorum (Buschke) Presented by DR A E WALKER and DR W MARMELZAT (service of DR H N COLE and DR J R DRIVER)

L S, a 51 year old Italian woman, had, approximately twenty months ago, a sudden onset of nonpruritic thickening and tightening of the skin of the neck, which spread to the lateral and anterior portions of the neck, the lateral aspects of the face, back, shoulders, upper arms and upper part of the chest The skin is softer now than it was after onset of the condition The patient has had previous episodes of infection of the upper part of the respiratory tract and influenza but no clearcut episode immediately preceding the onset of her present illness (There is a language barrier and a lucid history is difficult to obtain)

The patient has diabetes mellitus, which is being treated by diet and insulin She also has been treated medically for a hypertrophic arthritis Two years ago she had menorrhagia, the cause of which was never explained

There is painless, nonpruritic thickening of the skin of the back of the neck, extending over the dorsum to the iliac area, laterally around the neck to the anterior aspect, over the shoulders and upper arms to the deltoid area, and over the upper part of the chest and superior portion of both breasts The epidermis is not changed There is no pitting edema There are bilateral xanthelasma lesions

Urinalysis showed sugar (4 plus) and acetone (3 plus) The urea nitrogen was 18 mg per hundred cubic centimeters The fasting blood sugar was 303 mg per hundred cubic centimeters Total proteins were 6 3 Gm per hundred cubic centimeters—albumin 3 8 Gm and globulin 2 5 mg, combining power 52 5 milliequivalents per liter, blood cholesterol 354 mg, serum calcium 9 8 mg and serum phosphorus 4 3 mg per hundred cubic centimeters Results of hemocytologic studies were normal The blood and spinal fluid were normal The basal metabolic rate was +17 per cent Roentgenograms of the chest, sinuses, jaw and skull were normal

Biopsy of the skin revealed the epidermis to be normal The corium was thickened, made up of deeply acidophilic, greatly hypertrophied collagenous fibers The small vessels and capillaries were not remarkable but were surrounded by a moderate infiltration of lymphocytes and occasional polymophonuclear leukocytes No treatment has been given

DISCUSSION

DR H A BRUNSTING What is the duration of the disease?

DR R C LIGHT In the *New England Journal of Medicine* several months ago there was a report of a case of twenty years' duration

DR A E WALKER Another review I saw listed 1 case lasting thirty years and 1 four years The average is eight to eighteen months

Sarcoidosis (Granuloma Annulare [?] of the Elbows and Knees) Presented by DR A E WALKER and DR W MARMELZAT (service of DR H N COLE and DR J R DRIVER)

Sarcoidosis (Keloidal Lesions on the Nape of the Neck) Presented by DR A E WALKER and DR W MARMELZAT (service of DR H N COLE and DR J R DRIVER)

her closely but could get no history of the ingestion of arsenic I simply think that we have to decide whether this entire picture should be included in a single dermatologic entity, which I rather doubt at present

DR HAMILTON MONTGOMERY, Rochester, Minn I thought this was a case of congenital defect She has a flat nose You could not call it a congenital ectodermal defect with the changes in the tongue, but we have seen cases of endodermal and ectodermal changes merging together She did not have changes in the teeth but had changes in the palms that might indicate an ectodermal defect, as would the changes in the neck In addition she has apparently had a dermatitis which does not belong with that picture I would suggest that her family history be investigated

DR FRANCIS W LYNCH, St Paul, Minn I thought of the possibility of an ectodermal defect, but the mucosal changes were too great The family history is normal as far as could be learned on brief questioning

Darier's Disease (Keratosis Follicularis), Improvement Following Vitamin A Therapy Presented by DR S J ZAKON and (by invitation) DR A L GOLDBERG

A Case of Keratosis Follicularis with Cutaneous, Mucous Membrane and Nail Changes Presented by DR CLEVELAND J WHITE and (by invitation) DR ROBERT H HARRIS

A Case for Diagnosis (Drug Eruption? Neurotic Excoriations? Cutaneous Tuberculosis?) Presented by DR D V OMENS and (by invitation) DR H D OMENS and DR J GRAFFIN

A Case for Diagnosis (Sarcoidosis?) Presented by DR M H EBERT and (by invitation) DR ALLEN PEARL

Sarcoidosis Presented by DR STEPHEN ROTHMAN and (by invitation) DR EDWARD LADEN

Multiple Neurofibromatosis of Von Recklinghausen Presented by DR THEODORE CORNBLEET and (by invitation) DR D COHEN and DR J GRAFFIN

Multiple Neurofibromatosis Presented by DR EDWARD A OLIVER and staff of Hines Hospital

Rupial Syphilid Presented by DR D V OMENS and (by invitation) DR HAROLD D OMENS and DR N L BAKER

Secondary Syphilis and Granuloma Inguinale (?) Presented by DR JAMES R WEBSTER and DR S M BLUEFARB and (by invitation) DR N L BAKER.

Chronic Urticaria Due to Intestinal Organisms, "Giardia Lamblia", "Cure" Following Treatment with Quinacrine Hydrochloride Presented by DR JAMES H MITCHELL and (by invitation) DR ROBERT H HARRIS

Monocytic Leukemia, Schilling Type, Nodular Cutaneous Lesions Presented by DR G M STROUD

A Case for Diagnosis (Melanosis? Poikiloderma of Civatte? Chloasma?) Presented by DR A E WALKER and DR W MARMELZAT (service of DR H N COLE and DR J R DRIVER)

Rosacea-like Tuberculid of Lewandowsky Presented by DR W R HUBLER

George W Binkley, M D, *President*
George H Curtis, M D, *Secretary*
Gerard A DeOreo, M D, *Reporter*
Oct 23 1947

Congenital Ichthyosiform Erythroderma, Persistent Notochord Presented by DR M H GUSTAFSON, DR E H JONES JR and DR M UTTERBACH (service of DR J E RAUSCHKOLB and DR G A DEOREO)

Nonspecific Dermatitis, Associated with Lymphoblastoma Presented by DR M H GUSTAFSON, DR E H JONES JR and DR M UTTERBACH (service DR ROY W SCOTT)

Lymphangiectasis of Vulva, Secondary to Probable Tuberculous Salpingitis, Pulmonary Tuberculosis, Moderately Advanced Presented by DR M H GUSTAFSON, DR E H JONES JR and DR M UTTERBACH (service of DR J E RAUSCHKOLB and DR G A DEOREO)

A S, a 29 year old woman, was first seen on the dermatologic service in September 1947, complaining of pruritic lesions of the vulva, of four months' duration She said that they had gradually increased in size and that the pruritus had become much more pronounced in the previous three weeks, with some weeping of the lesions She noted that a watery material was obtained from the individual lesions if she pricked them with a needle

Both the labia majora and the labia minora are covered with acuminate, cystic lesions, which are slightly tender and moderately pruritic The lesions are tense and are filled with a thin, colorless fluid Large, nonpigmented, polypoid lesions surround the external anal orifice Numerous healed scars are present on the abdomen and thighs The anal sphincter admits the index finger only, with much pain The rectum, within the reach of the examining finger, exhibits no abnormalities Bronchovesicular breath sounds, with fine, post-tussic rales, are heard at the apex of the right lung

Reactions to a skin test with old tuberculin (1 100,000) were positive Those to the Frei test were negative The Kline and Wassermann reactions of the blood were negative Results of urinalysis and the hemogram were within normal limits The roentgenogram of the chest revealed moderately advanced pulmonary tuberculosis of the upper lobe of the right lung

Histologic examination showed that the papillary projections of the epithelium were elongated and that there were many clusters of lymphocytes and plasma cells scattered throughout the underlying stroma, especially about the capillaries Just beneath the epithelium there were many dilated lymphatic spaces

Folliculitis Decalvans (?) Presented by DR JAMES H MITCHELL and DR ROBERT H HARRIS (by invitation)

Folliculitis Decalvans Presented by DR F E SENEAR and staff

A Case for Diagnosis (Leprosy?) Presented by DR F E SENEAR

Linear Lichen Planus Presented by DR JAMES H MITCHELL and DR RALPH SCULL and (by invitation) DR BERNARD YATTE

Epidermolysis Bullosa Presented by DR F E SENEAR and staff

Widespread Morphea with Acute Development Presented by DR STEPHEN ROTHMAN and (by invitation) DR LOUIS RUBIN

Two Cases for Diagnosis (Unrelated), (Lichen Sclerosis et Atrophicus?) Presented by DR THEODORE CORNBLEET

Eosinophilic Granuloma Presented by DR EDWARD A OLIVER and (by invitation) DR E LORANT

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Eczema Vaccinatum Presented by DR F E SENEAR and staff

A Case for Diagnosis (Secondary Vaccinia [Autoinoculation]) Presented by DR F E SENEAR and staff

Penicillin was administered, with pronounced diminution of the secondary infection The patient was transferred to Sunny Acres, Cuyahoga County Tuberculosis Hospital, for treatment of her tuberculosis

A Case for Diagnosis (Granuloma Telangiectaticum?) Presented by DR M H GUSTAFSON, DR E H JONES JR and DR UTTERBACH (service of DR H R TRATTNER)

G S, a 50 year old man, was first seen on the urologic service in September 1947, with a complaint of numerous growths on the penis and the scrotum, of two years' duration The lesions started as a papule on the dorsum of the penis and gradually increased in number and size, finally involving the entire penis, the scrotum, the perineum and the perianal area The lesions have been asymptomatic

The patient gave a history of having had gonorrhea in 1929 A urethral stricture developed in 1932 In 1933 the first of a series of urinary fistulas appeared, and since that time numerous fistulas have developed around the base of the penis, the scrotum, the lower part of the abdomen and the perineum

The shaft of the penis, the scrotum, the perineum and the perianal area are covered with a fungating, polypoid mass The surface of the mass presents numerous flesh-colored nodules, pedunculated tumors ranging from a few millimeters to 3 cm in diameter Several fistulous openings may be identified in the crevices between the polyps Urethral strictures are present, preventing the passage of sounds

Results of urinalysis and the hemogram were normal The blood urea nitrogen was within normal limits The Kline and Wassermann reactions of the blood were negative Reactions to the Frei test and to skin tests for chancroid were negative An intravenous pyelogram revealed a normal right kidney and ureter, the left kidney was poorly visualized There was a slight hydroureter in the lower portion of the left ureter Suprapubic cystostomy revealed a normal bladder

Histologic examination showed stratified squamous epithelium, the seat of chronic inflammation, with fibrosis of the corium and areas of acute inflammation with focal ulceration

Treatment has consisted of the administration of penicillin and suprapubic cystostomy in preparation for plastic repair

DISCUSSION OF PRECEDING CASES

DR G A DEORDO I think that both of the preceding cases are manifestations of lymphostasis, associated with lymphatic blockage, in the woman due to tuberculosis and in the man resulting from obliteration of the lymphatics by some chronic inflammatory process associated with his gonorrheal infection Clinically at least, the growths looked like lymphangiomas, a form of elephantiasis Microscopically, the picture in the man looked considerably different There are many dilated capillaries or possibly lymphatics with thicker walls I should offer the diagnosis of elephantiasis or lymphangioma in both cases

DR F M MACDONALD I have never seen elephantiasis due to granuloma inguinale This is not the usual picture, but for the sake of work-up it is a very unusual situation I did not see any reference made to examination for possible Donovan bodies Perhaps that was done and I did not see mention of it on the report

DR J E RAUSCHKOLB The case of A S is a lymphostatic type of disorder, that contention is proved There are elevated little cystic lesions, and the lymphostasis probably arises from a chronic inflammatory pelvic condition, which we assume to be of a tuberculous origin

her closely but could get no history of the ingestion of arsenic I simply think that we have to decide whether this entire picture should be included in a single dermatologic entity, which I rather doubt at present

DR HAMILTON MONTGOMERY, Rochester, Minn I thought this was a case of congenital defect She has a flat nose You could not call it a congenital ectodermal defect with the changes in the tongue, but we have seen cases of endodermal and ectodermal changes merging together She did not have changes in the teeth but had changes in the palms that might indicate an ectodermal defect, as would the changes in the neck In addition she has apparently had a dermatitis which does not belong with that picture I would suggest that her family history be investigated

DR FRANCIS W LYNCH, St Paul, Minn I thought of the possibility of an ectodermal defect, but the mucosal changes were too great The family history is normal as far as could be learned on brief questioning

Darier's Disease (Keratosis Follicularis), Improvement Following Vitamin A Therapy Presented by DR S J ZAKON and (by invitation) DR A L GOLDBERG

A Case of Keratosis Follicularis with Cutaneous, Mucous Membrane and Nail Changes Presented by DR CLEVELAND J WHITE and (by invitation) DR ROBERT H HARRIS

A Case for Diagnosis (Drug Eruption? Neurotic Excoriations? Cutaneous Tuberculosis?) Presented by DR D V OMENS and (by invitation) DR H D OMENS and DR J GRAFFIN

A Case for Diagnosis (Sarcoidosis?) Presented by DR M H EBERT and (by invitation) DR ALLEN PEARL

Sarcoidosis Presented by DR STEPHEN ROTHMAN and (by invitation) DR EDWARD LADEN

Multiple Neurofibromatosis of Von Recklinghausen Presented by DR THEODORE CORNBLEET and (by invitation) DR D COHEN and DR J GRAFFIN

Multiple Neurofibromatosis Presented by DR EDWARD A OLIVER and staff of Hines Hospital

Rupial Syphilid Presented by DR D V OMENS and (by invitation) DR HAROLD D OMENS and DR N L BAKER

Secondary Syphilis and Granuloma Inguinale (?) Presented by DR JAMES R WEBSTER and DR S M BLUEFARB and (by invitation) DR N L BAKER

Chronic Urticaria Due to Intestinal Organisms, "Giardia Lamblia", "Cure" Following Treatment with Quinacrine Hydrochloride Presented by DR JAMES H MITCHELL and (by invitation) DR ROBERT H HARRIS

The case of G S is of a condition I have never seen before, however Clinically, this looks like the male counterpart of an esthiomene, in which there is a urinary passage in the perineal area There are thickening and chronic inflammatory changes in the rectum and exuberant fibrotic growths on the penis and the pubic area The condition has improved tremendously in the last months from simply a little plastic surgery and the use of penicillin to clear up the secondary infection The Frei test, skin tests for chancroid and serologic tests gave negative reactions We found no smear positive for fusiform bacilli of Vincent Unfortunately, the smear for Donovan bodies was not made because the case was not into our service, although we recommended that it be done The disorder has probably resulted from a long-standing gonorrhea in which there was a posterior stricture and a false passage which opened in the perineum, with extravasation of urine into the structures adjacent to it, chronic inflammation of the structures and secondary infection being produced The diagnosis of granuloma telangiectaticum pyogenicum probably was made because there was an infected granuloma, although clinically the tumor is not the pyogenic type

Psoriasis Arthropathica Presented by Dr M H Gustafson, Dr E H Jones Jr and Dr M Utterbach (service of Dr Roy W Scott)

Morphea or Lichen Sclerosus et Atrophicus(?) Presented by Dr M H Gustafson, Dr E H Jones Jr and Dr M Utterbach (service of Dr J E Rauschkolb and Dr G A DeOreo)

Multiple Benign Cystic Epithelioma, Alopecia Areata Presented by Dr M H Gustafson, Dr E H Jones Jr and Dr M Utterbach (service of Dr J E Rauschkolb and Dr G A DeOreo)

H D, a 44 year old woman, has four siblings, her mother and a sister have lesions similar to hers The patient has a daughter, aged 23, who is just beginning to exhibit similar lesions

Acrokeratosis Verruciformis Presented by Dr M H Gustafson, Dr E H Jones Jr and Dr M Utterbach (service of Dr J E Rauschkolb and Dr G A DeOreo)

W H, a 16 year old girl, was first seen in the dermatologic service in June 1947, with lesions on the hands and feet, which have been present since birth They have produced no symptoms and have not changed in size since puberty

The patient's aunt and father have had similar lesions since birth The patient was treated with penicillin therapy for secondary syphilis, ending Sept 19, 1947 She was hospitalized for acute and chronic pelvic inflammatory disease in 1946 She states that her parents are not related by blood

Over the proximal interphalangeal joints and the knuckles of both hands are multiple, firm, keratotic papules, measuring 2 to 8 mm in diameter Over the medial and lateral aspects of both palms and soles and the tendo achillis are multiple, small, discrete, firm papules

The roentgenogram of the chest showed normal conditions The results of urinalysis and the hemogram were normal The Kline and the Wassermann reactions of the blood were 4 plus, with a titer of 1 64

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Histologic examination showed pronounced hyperkeratosis, unusual prominence of the stratum granulosum, acanthosis and superficial chronic perivascular inflammatory infiltration of the corium

Since follow-up antisyphilitic therapy was instituted with bismuth subsalicylate, the patient says that the lesions have regressed for the first time

DISCUSSION

DR M UTTERBACH This patient gave a history of similar lesions in other members of her family, which I think is significant It is difficult to evaluate the lesions themselves We considered diagnosis of acrokeratosis, hydrokeratosis and perhaps linear nevus Biopsy showed definite proliferation of the corium Therefore we thought of the possibility of an acrokeratosis

DR H A HAYNES JR I have never seen a case like this, but the disorder could be verruca plana, inasmuch as it is undergoing involution with therapy

DR H J PARKHURST I thought that clinically on close inspection these do not appear to be ordinary warts They resemble the lesions in a case which I previously saw of epidermodysplasia verruciformis

DR G W BINKLEY It would be interesting to get a progress note on this case

Scleroderma, Acrosclerosis Presented by DR M H GUSTAFSON, DR E H JONES JR and DR UTTERBACH (service of DR J E RAUSCHKOLB and DR G A DEORIO)

George W Binkley, M D, *President*
George H Curtis, M D, *Secretary*
Gerard A DeOreo, M D, *Reporter*
Nov 20, 1947

Glossitis Rhomboidea Mediana Presented by Dr BENJAMIN P PERSKY

A Case for Diagnosis (Palmar and Plantar Keratoses [Arsenic?] [Keratoderma Disseminatum Palmaris et Plantaris]? Superficial Epitheliomas, Trunk Ulceration, Left Small Toe and Left Palm [Squamous Cell Epithelioma?]) Presented by DR B LEVINE, DR B PERSKY and DR I L SCHONBERG

A Case for Diagnosis (Ulcer, Penis, Cause Undetermined? Erythroplasia of Queyrat? Intraepidermal Epithelioma?) Presented by DR H H JOHNSON and DR I L SCHONBERG

J T, a Negro aged 32, was circumcised in February 1945, since which time there has been a superficial ulcer on the glans penis He has been hospitalized on numerous occasions since 1945 because of this penile lesion The treatment has included the administration of penicillin and numerous local medications, without any signs of improvement during this two year period

On admission to the service in May 1944 the patient was found to have a positive serologic reaction and was treated with a series of injections in the arm and the hip In 1945 he received 146 injections of penicillin because of the positive

CLEVELAND DERMATOLOGICAL SOCIETY

Harley A Haynes, M D, *President*

George W Binkley, M D, *Secretary*

March 27, 1947

Lymphogranuloma Venereum of the Shaft of the Penis, Nodules and Sinuses Presented by DR H H JOHNSON and DR A M TANNO (by invitation)

A Case for Diagnosis (Tuberculous Cervical Lymphadenitis? Lupus Miliaris Disseminatus? Tuberculid?) Presented by DR H H JOHNSON and DR A M TANNO (by invitation)

Pityriasis Rubra Pilaris? Presented by DR J KAM, DR R C LIGHT and DR A E WALKER (Service of DR H N COLE and DR J R DRIVER)

A Case for Diagnosis (Chronic Dissecting Cellulitis of the Groin and Left Foot Resembling Deep Mycosis?) Presented by DR J KAM, DR R C LIGHT and DR A E WALKER (Service of DR H N COLE and DR J R DRIVER)

Diffuse Progressive Scleroderma Presented by DR J KAM, DR R C LIGHT and DR A E WALKER (Service of DR H N COLE and DR J R DRIVER)

Perifolliculitis Abscedens et Suffoidiens Capitis (Hoffman) Presented by DR J KAM, DR R C LIGHT and DR A E WALKER (Service of DR H N COLE and DR J R DRIVER)

DISCUSSION

DR R C LIGHT There was pronounced improvement after the patient received two treatments of filtered roentgen rays

DR J R DRIVER I should like to ask whether any of the members have treated a condition of this kind with penicillin by injection and what the result has been

DR G H CURTIS I saw 2 patients in the Army treated with 8,000,000 units of penicillin without any benefit

DR H N COLE There were several of these patients at City Hospital, with chronic conditions They were given penicillin by injection and also treated locally with penicillin and penicillin irrigations, without any effect The disease in this case is relatively recent, which I believe is the explanation for the response

Severe Generalized Excoriations Associated with Jaundice (Possible Xanthomatous Biliary Cirrhosis) Presented by DR J KAM, DR R C LIGHT and DR A F WALKER (Service of DR H N COLE and DR J R DRIVER)

reactions to the serologic test for syphilis Numerous lumbar punctures have shown no abnormalities

His blood pressure is 154 systolic and 110 diastolic Examination of the genitalia reveals a 2 by 3 cm ulcer on the left side of the dorsal surface of the glans penis, extending down to the shaft The ulcer has a red, granulating base, partially covered by a thick, dry crust, and the edges of the ulcer are slightly thickened and rolled The lymph nodes are not remarkable

In June 1946 the reaction to the Kahn test was 4 plus, with 10 Kahn units, and reactions to the complement fixation test were negative, however, on two occasions in November the serologic reactions were negative Several urinalyses have shown a specific gravity from 1 010 to 1 022, and on several occasions there have been white blood cells with clumping Biopsy of the penile lesion showed acute inflammation of the skin, with ulceration and atypical hyperplasia of the epithelium An electrocardiogram showed an essentially normal record, with slight elevation of the S-T segment

A Frei test gave negative reactions, and no definite inclusion bodies were seen on the slide of the biopsy specimen The patient has concluded a course of streptomycin, consisting of 4 Gm a day for six days The only other medication has been warm saline compresses to the penile lesion On this therapy there has been definite healing at the periphery of the ulcer and the ulcer is now approximately 1 cm smaller in diameter

The following is the report of the microscopic examination "Examination revealed that the epithelium was ulcerated The ulcer was densely infiltrated with many lymphocytes and plasma cells Over the ulcer there were necrotic debris and many polymorphonuclear leukocytes There were islands of epithelial cells in which the nuclei were large and vesicular, and there were a few large, irregular, oval bodies, resembling somewhat a molluscum body Some of the epithelial cells showed metallic diversion The diagnosis was acute inflammation of the skin, with ulceration and atypical hyperplasia of the epithelium"

DISCUSSION

DR G A DEOREO I think that this man has granuloma inguinale The rapid improvement on treatment with a relatively short course of streptomycin also points toward this diagnosis It is true that there are certain findings in the biopsy which suggest pseudoepitheliomatous hyperplasia, but these changes are frequently seen in granuloma inguinale

DR J E RAUSCHKOLB The chronicity of the lesion, the lack of pain and the resistance of the disorder to ordinary antisyphilitic drugs point, as Dr DeOreo says, to pseudoepitheliomatous hyperplasia, but the condition is not neoplastic in character, and it cannot be anything else but granuloma inguinale One ought to be able to find Donovan bodies, however

DR H N COLE This is a very interesting case One hesitates to make two diagnoses if one will suffice I have seen sections from a large number of cases of granuloma inguinale, and I have seen several examples of pseudoepitheliomatous hyperplasia, but I have never observed anything like the condition this man presents, as seen in the section I do not see how one can avoid calling this disorder intraepithelial carcinoma as well as granuloma inguinale Of course, in Negroes one does not very often see epitheliomatous changes on the skin, but this section shows such a remarkable picture that I do not see how we can refuse to make that diagnosis It would be interesting to have another report on this patient later

1 Boeck's Sarcoid 2 Early Latent Syphilis, Partially Treated Presented by DR J KAM, DR R C LIGHT and DR A E WALKER (Service of DR H N COLE and DR J R DRIVER)

A Case for Diagnosis (Dermatitis Repens?) Presented by DR H H JOHNSON and DR A M TANNO (by invitation)

Alopecia Liminaris Frontalis (Sabouraud) Presented by DR J KAM, DR R C LIGHT and DR A E WALKER (Service of DR H N COLE and DR J R DRIVER)

F W, a Negro woman aged 28, first noticed mild acne of the face and the gradual onset of alopecia of the frontal region of the head in October 1945 Within several months this reached its peak and has persisted to the present There is no history indicative of an endocrine disturbance She has used petrolatum on her hair for many years There is no family history of similar disease

Results of a general physical examination were normal, and she appears in good condition In the frontal portion of the scalp there is a symmetric, well defined band which is almost completely devoid of hair This extends from ear to ear and 3 to 5 cm back of the hair line There is conspicuous plugging of the follicles throughout, and the skin is slightly depressed, suggesting atrophy No erythema is seen There is mild papular acne of the face

Observations in hemograms and urinalyses were normal The result of the serologic test for syphilis was negative The basal metabolic rate was +16 per cent

On histologic examination, the epithelium showed no significant change There was a scattered infiltrate of lymphocytes, histiocytes and pigmented mononuclear cells in the upper part of the corium and to a lesser extent in a few deeper areas around the hair follicles Keratotic plugs often blocked the mouth of the follicles, which frequently contained no hair A trial course of 100,000 units of vitamin A daily for two months had no objective effect

DISCUSSION

DR H G MISKJIAN I have been interested in this subject for some years, after I read a long description of the syndrome given in the *Annales de dermatologie et de syphiligraphie* in 1931 by Sabouraud, in which he said that he had seen 12 cases of this disease in thirty years In the last ten or more years my co-workers and I have, here at the Lakeside Clinic, seen at least 10 or 12 cases, which were all in Negro women, and as far as I remember, all of them were in adults Sabouraud saw his cases in girls of acne age, about 15 to 18, and he mentioned a woman about 50 years old who had it, I have brought the book in which the picture of that woman appears This shows that there are differences between what Sabouraud reported and what we have seen here One of the differences is that in the syndrome we have seen the disease seems to be much more frequent than Sabouraud reported The second point of difference is that our cases are in adults and Sabouraud's were almost entirely in adolescents A third difference is in frequency, we have seen them much more frequently at our clinic The description seems to correspond closely with that of Sabouraud A patch of alopecia would develop on each preauricular temporal region, which would secondarily spread onto the forehead, toward the midline, with a band of alopecia about 1 inch (2 5 cm) or a little less Right on the fringe of the forehead and the band of alopecia there is usually a thin line of hair The patient presented today had that also The alopecia is supposed to be permanent, once it has been estab-

Keratosis Follicularis (Darier's Disease) Improvement After Therapy with Vitamin A Presented by DR E L GLICKSBERG

A Case for Diagnosis (Erythema Elevatum Diutinum? Eosinophilic Granuloma?) Presented by DR I L SCHONBERG

S F, a white man aged 62, first noted swellings on the head and the left arm in 1926 At that time he was treated with various methods, including roentgen irradiation and use of solid carbon dioxide After the application of the solid carbon dioxide an ulcerated area, which required many months to heal, developed on the scalp Since that time the patient has acquired new tumors on the left part of the chest and on the nose These have grown slowly and have darkened About three months ago several nodules were removed surgically from the left breast and the left arm The lesions have been asymptomatic

General physical examination showed essentially normal conditions On the front and the left side of the nose there are two nodules, one the size of a bean and the other the size of an almond The tumors are sharply demarcated, reddish brown and firm to palpation On the left arm there are two dollar-sized areas of atrophy, at the border of which there are pea-sized to bean-sized violaceous nodules There is an atrophic, circular scar, 6 cm in diameter, on the scalp

Treatment has consisted of irradiation with filtered roentgen rays, without results

The results of urinalysis were normal, as was the examination of the stools The hemogram revealed 5,200,000 red blood cells, 10,000 white cells, and 13 Gm of hemoglobin, with a differential count of 62 per cent polymorphonuclear cells, 38 per cent lymphocytes and no eosinophils Testing for allergic reactions gave negative results

A biopsy specimen taken from the wall of the chest showed in the dermis and underlying subcutaneous tissue a circumscribed nodule, measuring about 1 cm in long diameter The central portion of the nodule was composed of dense bundles of collagenous fibers, which were diffusely infiltrated by wandering cells Toward the periphery of the nodule the blood vessels were prominent and considerably increased in number and showed pronounced perivascular infiltration by wandering cells, among which eosinophils predominated The most characteristic changes appeared to be at the base of the lesion in the subcutaneous fat, with vessels thickened there, the media showed slight infiltration by eosinophils, and the regional stroma showed intense infiltration by wandering cells, among which eosinophils predominated

At one edge of the nodule in the dermis there were large bundles of smooth muscle, apparently hypertrophied smooth muscle of a tortuous artery The epidermis was thinner than average, and interpapillary projections were obliterated There was a moderate amount of brown granular pigment in the basal epithelial cells

A second biopsy specimen, taken from the arm, showed a similar picture, but with less advanced sclerosis of the central portion of the nodule than was seen in the material from the wall of the chest At the base of the lesion there was a thick-walled blood vessel In the lesion itself there are numerous blood vessels showing intense cellular infiltration of the vascular wall and perivascular tissue, in which eosinophils predominate

Section stained by the azocarmine method showed an increase in blue-stained fibrous tissue, especially in the lesion from the chest wall, and abundant red-stained smooth muscle bundles in the area, suggesting tortuous or aneurysmal blood vessels in the dermis

lished, and one is supposed to see in the bald area small cicatricial lesions, which I was not able to see in this case I think it would be a very worth while contribution to bring together all of these cases to study them and point out that this syndrome is perhaps more frequent in the Negroes than in white person Nothing is known about it, because Sabouraud seemed to think that the syndrome must be placed between what he calls staretoid baldness, in other words alopecia, and an acneform process, because in the early stages he was able to see acne lesions in areas which later became bald There is a good description of this syndrome in Dr Sutton's book, "Diseases of the Skin," which is accurate

DR J A GAMMEL A few months ago I had a Negro woman patient with what I called alopecia areata, limited to the same areas, which cleared up very well in three months

DR H G MISKJIAN When this patient first came to us we considered the diagnosis of alopecia areata, because the case was not so very characteristic, and we ruled it out at that time At the present time the appearance is not that of alopecia areata There are thin areas that one would ordinarily not see in alopecia areata

DR J A GAMMEL I do not want to make a diagnosis in this case, but merely comment that I saw one with the disease limited to these areas There was complete baldness for two weeks, and in three months the whole process was over

DR H H JOHNSON There is one thing that Negro women do that is peculiar to their race, and that is using various methods of attempting to straighten hair I believe that that should be investigated thoroughly to find out what methods they use to accomplish it

A Case for Diagnosis (Lichen Planus Atrophicus? Chronic Atrophic Lichenoid Dermatitis [Csillag]? Retiform Parapsoriasis?) Presented by DR G W BINKLEY and DR H H JOHNSON

Papulonecrotic Tuberculid Presented by DR J KAM, DR R C LIGHT and DR A E WALKER (Service of DR H N COLE and DR J R DRIVER)

Harley A Haynes, M D, *President*

George W Binkley, M D, *Secretary*

May 22, 1947

Herpes Gestationis Presented by DR W R HUBLER, Youngstown, Ohio

DISCUSSION

DR J E RAUSCHKOLB This patient has neither oral nor ocular lesions She is two or three months pregnant In spite of this eruption having followed the beginning of pregnancy, I believe that the case is one of pemphigus vegetans because of the extreme prostration and toxicity and the grouping of the bullae on the neck band and axillary and genital areas, which are beginning to pile up and vegetate

DR C G LA ROCCO I agree with Dr Rauschkolb

DR J R DRIVER I agree with the diagnosis as presented There was no Nickolsky sign The woman is pregnant and has had this eruption since her pregnancy started A therapeutic abortion is indicated

DISCUSSION

DR G H CURTIS Clinically, the disease looked like sarcoidosis

DR B LEVINE I saw this man some years ago, and I thought at that time that he had sarcoidosis Many other dermatologists have seen him since

DR G A DEORIO In the 2 cases of erythema elevatum diutinum that I have seen, the edges of the lesions were more perpendicular than they are in this case and the surface formed a plateau The color was not quite as intense as in this case, and the microscopic picture was considerably different from the one we see in this case I should like to suggest the possibility of Kaposi's hemorrhagic disease

DR B PERSKY I should not quite agree with the diagnosis of eosinophilic granuloma here because of the absence of large cells either in the skin or in the bone There were quite a few eosinophils, but I do not think they would add up to the number seen in eosinophilic granuloma I have had occasion to deal with a case of erythema elevatum diutinum, with the characteristic features This case showed ring-shaped lesions around the digits and around the joints, quite blue but not as deeply blue as the lesions in the present case The lesions here somewhat resembled granuloma in that they had a smooth surface and an annular configuration They did not show the picture of granuloma annulare histologically There is one other possibility which I should like to suggest I am not at all sure how accurate the history is I should like to suggest the possibility of periarteritis nodosa There were some vascular changes I think that more biopsies might reveal those features, and possibly further observation and a fuller history as to whether there were remissions or relapses might help

DR I L SCHONBERG When I saw this patient for the first time I was very confused, as you might expect, and on going over his history there were several things that I thought of I was hoping that when I made the biopsy the diagnosis would be sarcoid, but unfortunately it could not be made on the section However, there was a new lesion at the base of the left breast, and we also decided to take a border specimen from the lesion of the left arm On pathologic examination, the condition was reported as periarteritis nodosa I do not feel that the disorder falls in that class, at least clinically On reading the literature, I became more and more confused as to whether or not it fitted in with that diagnosis In the February 1947 issue of ARCHIVES, pages 155 to 201, there are three or four articles on erythema elevatum diutinum and eosinophilic granuloma The examination of the section did not reveal a picture fitting into the type of erythema elevatum diutinum as described by the first author, but observations did fit in with the picture described by Weidman He stated that erythema elevatum diutinum presents a polyarteritis with a cellular infiltrate He quoted an Italian dermatologist, who described a case almost identical with the one I have shown He described lesions on the extensor surface of the hands, the ears, the face and the buttocks According to some of the descriptions, many of these cases began in early life However, there was a group of cases in persons usually over 40 years of age, who presented similar lesions Two types were described the "Hutchinson type," or soft type, with soft plaques, and the "Bury type," with hard nodules which undergo a purplish discoloration There is also a third type, which resolves by itself It is rather difficult to classify this case, but I do feel that there are some indications that it fits into one group or the other

DR S J ZAKON I wonder whether dilantin® is responsible for the hyperplasia or the poor oral hygiene of epileptic persons I had 1 case of this type which I referred to the dentist for oral prophylaxis, and the hypertrophy subsided in spite of the patient's taking dilantin®

DR STEPHAN ROTHMAN I saw a severe generalized hemorrhagic toxic eruption following the use of dilantin,® but the patient did not display hypertrophy of the gums

DR E M SMITH JR This patient was examined by several dentists, who readily agreed that the hypertrophy was a typical result of the long-continued use of dilantin® sodium and that such cases were moderately common in their experience

Dermatomyositis with Slightly Lichenified Lesions on Exposed Surfaces Presented by DR F E SENEAR and STAFF

Lymphocytoma Presented by DR O H FOERSTER, DR H R FOERSTER and (by invitation) DR D M RUCH

D E, a white woman aged 38, had a "pimple" on the right lateral aspect of the forehead in 1938 which she picked and scratched This became hard and raised and remained pea sized until 1945 Since then it has grown gradually, until it is now about four times its original size In 1942 a similar lesion appeared suddenly on the right side of the forehead above the original lesion, and in April 1946 a third similar lesion appeared lateral to the first one Neither of the latter two lesions have changed in size or appearance

On the right lateral aspect of the forehead, 2 cm above the lateral supraorbital margin, is a smooth, firm, cutaneous nodule, elevated about 4 mm Two similar round 5 mm lesions are also present, one 2 cm lateral to the former lesion and the other 0 5 cm above it

Histologic examination showed acanthosis to be present in some areas of the epidermis, and there was condensation in the collagen of the subpapillary layer Areas of lymphocytic infiltrates together with a few plasma cells were present about the glandular structures and in circumscribed areas deep in the corium

A blood cell count (March 18, 1947) showed hemoglobin 90 per cent, leukocytes 7,870, erythrocytes 4,590,000 and color index 1 00 The differential count showed 65 per cent neutrophils (2 per cent nonsegmented and 63 per cent segmented), 2 per cent eosinophils, no basophils, 30 per cent lymphocytes (large 1 per cent, small 29 per cent) and 3 per cent monocytes The blood smear was normal

DISCUSSION

DR M R CARO This patient presents a condition which is difficult to diagnose clinically 'The most obvious diagnosis clinically would be sarcoid, but on histologic examination these small accumulations of lymphocytic cells without any inflammatory reaction are diagnostic for lymphocytoma In the cases reported in the literature there are no observations in the blood stream to make this condition of more serious prognosis I recall a patient presented about ten years ago before this society with a lesion under the eye identical with that in the present case The lesion disappeared after three or four fractional doses of roentgen rays without any recurrence

DR ADOLPH ROSTENBERG JR (by invitation) In the eleventh supplement to 1943 Acta dermato-venereologica there is an article on lymphadenosis benigna cutis There is a fine English summary In lymphadenoma there are two varieties,

in one there are isolated lesions such as this patient apparently has In the other variety there are multiple lesions, but in both the prognosis is about the same There is rarely systemic involvement An isolated cyst as this can arise at any age, whereas the generalized disseminated form is more often in elderly persons The author expressed the belief that a variety of stimuli are etiologic

DR HARRY FOERSTER, Milwaukee We presented this patient chiefly because of the frequency with which lesions of this type are misdiagnosed when they are not subjected to histologic study When first seen by us, the nodules appeared nevoid The history of progressive growth with appearance of new lesions in recent years, one as recently as nine months ago, suggested the possibility of endothelioma Sarcoid and sarcoma were also considered

Dr Caro made the diagnosis of lymphocytoma and also prepared the sections that were shown here today This patient received roentgen treatment about six weeks ago, and the lesions have been reduced about one third in size The pigmentation noted was caused or intensified by the roentgen therapy At the time this patient was being studied, we saw a woman with a similar lesion, and in the same site, which was shown to be an endothelioma on histologic examination

Albright's Syndrome (Fibrous Dysplasia of Bone, Precocious Puberty and Café au Lait Spots) Presented by DR F E SENEAR and STAFF

Francis W Lynch, M D, *President*

Leonard F Weber, M D, *Secretary*

April 16, 1947

A Case for Diagnosis (Streptococcic Eruption on the Face? Seborrheic Dermatitis?) Presented by DR JAMES HERBERT MITCHELL and (by invitation) DR ROBERT M GOODWIN

Pulsating Hemangiomas, Hepatic Cirrhosis Presented by DR T CORNBLEET and (by invitation) DR H SCHORR and DR J GRAFFIN

C D, a white woman aged 52, entered a medical ward at the Cook County Hospital on March 10, 1947 At this time she was given the diagnosis of cirrhosis of the liver with jaundice and ascites She was unable to give a history concerning the dermatitis of her forearms or the telangectatic lesions of her hands and face

Examination reveals a pulsating split-pea-sized lesion in the center of telangectasia on the right cheek The dorsum of the left hand has four smaller pulsating hemangiomas with a keratotic surface Both forearms and lower legs have a fairly well defined dermatitis The abdomen and chest show prominence of the superficial veins, and there are numerous telangiectases There is moderate ascites and icterus of the scleras Her temperature, while in the hospital, has steadily dropped from 102 to 99 F

The Kahn reaction of the blood was negative Repeated urinalyses revealed only a pronounced urobilinogen content The examination of the blood showed hemoglobin 58 per cent, erythrocytes 3,100,000 and leukocytes 8,100 The icterus index was 25 and 14 units The total protein was 6 1 Gm per hundred cubic centimeters, albumin 16 and globulin 4 5

The result of the cephalin flocculation test was 4 plus The nonprotein nitrogen was 31 mg per hundred cubic centimeters

MANHATTAN DERMATOLOGIC SOCIETY

David Bloom, M D, *Chairman*

Wilbert Sachs, M D, *Secretary*

March 11, 1947

Erythroplasia of Queyrat Cured. Presented by DR E W ABRAMOWITZ

W L is a white man aged 42, born in the United States, married, with one child He works as a supervisor at a paper manufacturing company

He first came under my observation on Sept 20, 1945 He presented weeping, erythematous patches on the glans penis and the shaft Around this area there were numerous areas of telangiectasia said to have followed roentgenologic therapy to the affected areas, with no apparent effect on the original lesions The duration of the eruption was three and one-half years

He failed to respond to ordinary topical remedies such as Aloe vera pulp and ointment, penicillin or various soothing applications prescribed by other dermatologists and by me I finally resorted to a proprietary preparation containing menthol, phenol, camphor, oil of cloves, oil of eucalyptus and lime water in a vanishing cream base of undisclosed formula Since this has been used, the eruption has healed and the patient has had no further trouble The telangiectasia has remained His wife has recently given birth to another child

DISCUSSION

DR JACK WOLF I think that this is an interesting and important case We have seen patients who have been cured, at least temporarily, with radiation, the improvement extending over several years Spontaneous remissions also probably occur in the course of the disease Apparently we do not as yet have the complete picture of the rationale of treatment or of the cure of erythroplasia of Queyrat

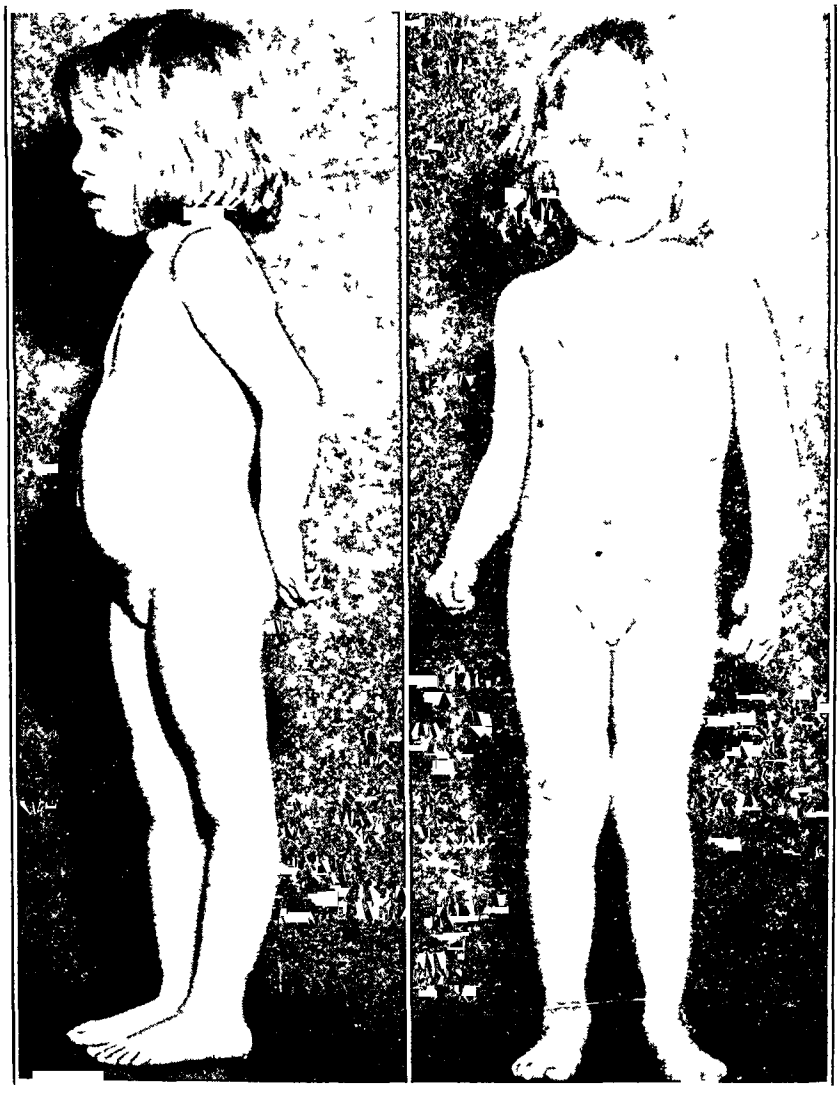
DR PERRY M SACHS (by invitation) I should like to know the time relationship between the roentgen treatments and the local therapy

DR GEORGE C ANDREWS I accept the diagnosis in this case, but I think that generally we have to be cautious about accepting the diagnosis of erythroplasia I have in mind a patient whom I saw about two years ago He had had a penile eruption for about two months It was diagnosed as erythroplasia after biopsy by Army physicians On questioning him I found that he had taken sulfadiazine a month or so before the eruption began I told him that I would not accept the diagnosis of erythroplasia and gave him a mild lotion to use, and the balanitis cleared up entirely without any other treatment It is possible that the sulfonamide drugs produce eruptions something like erythroplasia at times We do not know what causes erythroplasia It may come from different things in different persons, so what cures one may not necessarily cure another When carcinoma is definitely present, it is a different matter The whole subject is rather involved

DR NATHAN SOBEL These are interesting cases, and the condition is sometimes difficult to diagnose, as Dr Andrews and others have said When we see

DR JOHN G DOWNING I rubbed my finger nail on the leg After a few minutes a wheal appeared I think that it is a case of urticaria pigmentosa Whether this lesion belongs to the nevoid group, I do not know, other cases of urticaria pigmentosa are so classified

DR BERNARD APPEL, Lynn, Mass The histologic examination should have revealed a typical infiltrate if this were urticaria pigmentosa



Pigmented lesions in a 4 year old girl

Multiple Epidermal Cysts of the Skin Presented by DR MAURICE M TOLMAN, Boston

A 29 year old white nurse, S C, is presented with lesions on the back of her hands of six months' duration She first noted dermatitis venenata on the knuckles of both hands from handling a patient's flowers This was an acute vesicular eruption which healed with mild therapy but left behind small white nodular lesions Four months ago she received roentgen therapy, 500 r in divided doses This caused increased redness and tenderness, there was no improvement in the nodular lesions In the last few weeks they have become somewhat less prominent without further therapy

a patient apparently cured, we are inclined to question the diagnosis I think we must accept the fact that this patient has had erythroplasia and try to give credit where it is due

DR E W ABRAMOWITZ I am sure that Dr Sachs will bring out other important features of this disease Erythroplasia was always considered a serious disease, a precancerosis Radical measures, even including amputation, were discussed I do not recall ever seeing a patient with erythroplasia of the penis in whom cancer of the penis developed I have wondered, therefore, whether radical measures were justified In this case, roentgen rays apparently had no effect except to produce telangiectasia I tried to treat this telangiectasia because in the beginning it seemed to bother the patient He was able to tolerate mild applications of solid carbon dioxide to the telangiectatic area I soon stopped that, however, and used mild boric acid ointment and solution, Aloe vera pulp and then ointment, with little improvement It was not until Dr Cipollaro showed a patient with erythroplasia who had responded to this proprietary preparation that I told my patient about it and suggested its use The patient reported immediate relief I think one can say now that this lesion is healed There has been no activity for several months

I should like to mention another patient, brought to me by a urologist who was considering the possibility of radical measures, there was an erosive lesion of the penis which he thought was cancer I thought it was a drug eruption, as the lesion was typical of a fixed eruption I questioned the man about phenolphthalein, and he denied taking it I was so convinced that he was lying that I went to his house and found feen-a-mint® (laxative containing phenolphthalein) packages and wrappers When he stopped using this the ulcerations disappeared It is not unusual to see lesions in the mouth and on the penis from phenolphthalein, and I have seen a fixed eruption on the penis and in the mouth from veronal® (barbital U S P) and other barbiturates

Erythroplasia—Cured Presented by DR WILBERT SACHS

E G K, a white man aged 45, first noticed a small red papule on the glans penis two and one-half years ago This grew until almost the entire glans was involved There was continuous oozing and slight itching The patient had been treated by several competent dermatologists, all of whom had made a diagnosis of erythroplasia Therapy consisted of local applications of various preparations and the use of roentgen rays, radium and hormone injections, with little or no results

Laboratory examinations, including blood counts, urinalysis and serologic tests, revealed no significant findings Microscopic examination confirmed the diagnosis of erythroplasia

When first seen by us in December 1946, the patient had an erythematous, shiny, oozing patch over most of the glans penis There was no scaling or crusting and no induration The following medication was applied locally, twice a week, for three weeks 0 3 Gm of neoarsphenamine dissolved in 4 cc of distilled water, to which 1 cc of glycerin is added

Oozing and all subjective symptoms disappeared within one week The lesion became crusted, and in the following few weeks the entire process disappeared, leaving no sequelae

Examination reveals an eruption limited to the dorsa of the hands and distributed over the region of the metacarpophalangeal joints The lesions consist of numerous solitary and grouped, milky white, hard nodules of uniform size, they are all 1 to 2 mm in diameter A few exhibit a faint narrow rim of surrounding erythema There is no tenderness now

A specimen was removed for histologic examination, and the diagnosis of "multiple epidermal cysts" was made Results of examinations of the chemical content of the blood, including calcium, cholesterol esters and fatty acids, were normal

DISCUSSION

DR MAURICE M TOLMAN The biopsy specimens were studied in several laboratories, all with the same diagnosis epidermal inclusion cysts, with some changes in the elastic tissue There was no evidence of xanthomatous infiltrate, or of colloid, as far as we know In the literature are reports of 3 such cases Ormsby presented one (Ormsby, O S Bullous Dermatitis [Pemphigus?], ARCH DERMAT & SYPH **28** 246 [Aug] 1933) associated with pemphigus The lesions were in an area of the skin where pemphigoid lesions had healed, leaving these cysts In another instance, cysts came where there was vesiculation following exposure to the sun (Dietel, F *Dermat Wchnschr* **99** 1637, 1934) The third patient had lesions at the sites of vesicles probably from dermatitis venenata We have all seen this occur in epidermolysis bullosa Apparently what takes place is a peculiar reaction to trauma The vesicular lesions heal entirely, and it is in the healing areas that one finds the origin of these epidermal cysts, representing some peculiar response of the tissue The patient is now improving, and we cannot find any reason for it, although she is now pregnant It might be that with the hormonal reaction there may be a nonspecific response She is about 50 per cent better

DR FRANCIS P MCCARTHY The histologic slides showed typical epidermal cysts which are seen so often in the lesions of epidermolysis bullosa One can explain the development of epidermal cysts in the latter disease but not so easily in a vesicular dermatosis on the basis of trauma

Tuberculosis Miliaris Disseminata Faciei Presented by DR FRANCISCO RONCHESE, Providence, R I

Berlock Dermatitis in the Form of a Band Across the Forehead Presented by DR G MARSHALL CRAWFORD, Boston

DISCUSSION

DR MAURICE J STRAUSS, New Haven, Conn I do not recall from the history that a perfume had been used, but, even if it had been, this should not be labeled Berlock dermatitis I would call it pigmentation following dermatitis The term Berlock dermatitis was coined to describe the disease in cases where perfume had been poured on and allowed to run down The word Berlock means pendant It is that particular configuration in which there is evidence of an irritating substance running down in streaks which should be kept as the original concept of Berlock dermatitis

DR WILLIAM B SWARTS, Greenwich, Conn The patient said that he had been employed as a bartender and that the eruption started in September I asked whether he served many Tom Collins drinks during the summer, because the use of lime oil is important The mechanism is the same as Berlock dermatitis except that the essential oil is sprayed over his face A patient of mine with dermatitis venenata of the face made the diagnosis herself and stated that she never got the

DISCUSSION

DR NATHAN SOBEL It is an excellent result

DR JACK WOLF I think that Dr Sachs is to be congratulated It is the first opportunity that we have had of seeing any of the patients whom he has been treating We must take cognizance of the fact that this is not the only case he has shown tonight in which he has obtained a good result but that he is reporting a series of 10 cases, all of which he has followed assiduously Dr Abramowitz' case, which was reported tonight, and the instances of spontaneous improvement that we have seen do not detract in any way from the excellent work which Dr Sachs has done It adds an excellent method of treatment for a disease with which we have had so much trouble

DR MAX SCHEER I wonder whether the patients whom we have seen in this country with the disease which we label erythroplasia are suffering from what the French call erythroplasia According to the French authors, it is not only a precancerosis but it is a cancerosis and it invariably ends with metastasis to the inguinal lymph nodes and death In fact, there have been reports of cases in which the first lesion was a malignant process of the lymph node, followed later on by the erythroplasia of the glans penis In view of the fact that all the French cases have resulted in cancer unless radical treatment was performed and in view of the fact that, according to Dr Sachs, cancer has not developed in a single one of our patients, I wonder whether we are dealing with the same disease or whether it is contact dermatitis or some other kind of dermatitis, as Dr Rosen has suggested

DR PERRY M SACHS (by invitation) Whether or not we are dealing with the erythroplasia described by Queyrat is of secondary import It is erythroplasia as seen and diagnosed by dermatologists in this country and a disease which has proved resistant to all forms of therapy short of heroic measures

DR DAVID BLOOM I should like to ask Dr Sachs how he came to think of this treatment?

DR JACK WOLF Regardless of whether or not we are dealing with the disease which the French authors described, it must be admitted that if Dr Sachs has had such excellent results in the type of disease we see and which we call erythroplasia it is an important contribution to the therapy of a troublesome and obstinate disease We should be able to decide in the near future whether it is the same disease as that described by Queyrat

DR GEORGE C ANDREWS I had 1 case of erythroplasia, clinically typical and diagnosed microscopically by Dr Machacek, in which epithelioma of the penis developed and the patient died of metastasis

DR GEORGE M LEWIS Dr Sachs has observed 10 cases, which is probably 9 more than Queyrat had Why should we necessarily perpetuate Queyrat's conception unless it is the same as ours? I would support Dr Sachs's opinion over that of any of the foreign observers His cases are those in which we are interested It may be a different disease from the one described abroad, but it is the one that we see Furthermore, I think his treatment has been effective, and until this time our treatment has been poor Dr Sachs deserves a great deal of credit, obviously, he has controlled his work and has tried a great many remedies It is not something he thought of last week—he has been at it for a long time I think it is good work, he has not found the cause, but that is not always essential There are many diseases in which treatment is effective although the cause is unknown

eruption until the oil that caused the dermatitis was carried by the effervescent soda water to her face Wiley Sams (ARCH DERMAT & SYPH **44** 571, 1941) reported a case of dermatitis based on the photodynamic action of lime oil

DR JOHN G DOWNING This patient has used nose drops which may have contained silver nitrate Silver nitrate is precipitated rapidly by sun I have seen cases in Florida similar to these after exposure to the sun

DR JOSEPH GOODMAN The patient used a silver salt eighteen years ago for gonorrhea

DR WALTER F LEVER The histologic sections show no evidence of argyria If the pronounced darkening of this patient's skin were due to argyria, one should be able to see silver granules in the sections even without resort to dark field illumination There is considerable increase of melanin in the basal layer and an abundance of melanin-laden chromatophores in the upper part of the corium I regard this case, from the histologic point of view, as one of hyperpigmentation

DR JOHN G DOWNING These patients always exhibit pronounced pigmentation if they are exposed to excessive sunlight Argyria will increase this tendency

DR WILLIAM R HILL I was not impressed with the possibility of argyria, although I did not examine the patient's nails and conjunctivas I agree with Dr Lever histologically, there was too much pigment to suggest argyria Such pigment is found around the sweat glands

DR BERNARD APPEL, Lynn, Mass I was impressed not only by the streak across the forehead that resembled hat band dermatitis but also by the discoloration of the face and neck Melanosis of Riehl should be considered In questioning this man about his diet, I found that he practically never ate any fresh vegetables or fruits I think that there is a possibility of this being the dietary deficiency type of pigmentation which Riehl originally described This is also consistent with the microscopic picture

DR G MARSHALL CRAWFORD By common usage, I think that the term Berlock dermatitis has come to represent almost any bizarre pigmentary deposit caused by photosensitizing agents on the skin It is difficult to see how such a sharply defined rectangular patch could be created without a pattern contact such as a hat band The dye therein, or tanning chemicals, might be incriminated

A Case for Diagnosis (Bacterid?) Presented by DR JOSEPH GOODMAN, Boston

Mycosis Fungoides in a 56 Year Old Woman Presented by DR MAURICE M TOLMAN, Boston

Mycosis Fungoides in a 46 Year Old Man Presented by DR MILDRED L RYAN, Brockton, Mass

DISCUSSION OF CASES OF MYCOSIS FUNGOIDES

DR MAURICE J STRAUSS, New Haven, Conn The woman has changes on her tongue Dr McCarthy pointed them out and said that they were lesions of mycosis fungoides, he had seen a similar case I have never before observed this and wonder whether it would be possible to have a biopsy done to prove it

DR FRANCIS P MCCARTHY Textbooks on dermatology and oral medicine show plates of tongue lesions in mycosis fungoides About twenty years ago I saw a tongue which presented lesions of mycosis fungoides, somewhat like those on this woman's tongue The lesions were raised and nodular, the largest was 0 5 by

DR JACK WOLF Dr Sachs says that his therapy produces an adherent crust which remains for a long time Does he think, then, that we can achieve more rapidly the same type of crust and destruction by desiccation with the high frequency current or by the use of acids such as trichloroacetic acid? Is there any essential difference?

DR FRED WISE I am in complete accord with what Dr Lewis has said, but I think it would be not only desirable but necessary for the author to state that he is not sure he is dealing with the identical disease described by Queyrat American readers regard the term erythroplasia as meaning erythroplasia of Queyrat, and I suggest a notation to the effect that Dr Sachs is not sure he is dealing with that entity but that he is dealing with a disease similar in appearance and in chronicity, which, however, does not eventuate in cancer

DR DAVID BLOOM Neoarsphenamine dissolved in distilled water and then in glycerin, in 10 per cent concentration, has been used for several decades in the treatment of Vincent's infection of the mouth It is logical to assume that the beneficial effect obtained by Dr Sachs in his cases of erythroplasia is due to the effect on spirochetes or bacteria In these cases, therefore, there should be bacteriologic examination, irrespective of their duration

DR GEORGE M LEWIS I wonder if some of the malignant processes that supervene in these cases are the result of the treatment administered, such as desiccation or the use of pastes and irritant remedies In your opinion, Dr Sachs, is treatment ever responsible for malignant changes?

DR WILBERT SACHS The disease treated in this case, and in the other 9 cases reported in our paper, is the same as that described by Queyrat The French authors believe that in most of the cases the lesions become malignant The experience in our cases is not in accord with this view There have been only 2 cases reported in the American literature in which malignant changes developed In 1 the original diagnosis was questioned, in the other, the lesion was basal cell epithelioma and not erythroplasia Dr Andrews' case would make a third There are cases in which the lesion has all the clinical features of erythroplasia but microscopically proves to be either basal cell epithelioma or Bowen's disease However, as Dr Lewis suggests, it is always possible for a malignant process to follow long-continued treatment which includes such heroic measures as those employed in an endeavor to control erythroplasia In reply to Dr Wolf's question, desiccation and escharotic preparations have produced good results in some cases, but with sequelae and disfigurement These have not followed the treatment we are reporting

A Case for Diagnosis (Poikiloderma Atrophicans Vasculare?) Presented by DR DAVID BLOOM

R C, a white woman aged 47, complained of an eruption on the palms and soles of eight months' duration and of a generalized eruption of five months' duration The family history and the past history was essentially irrelevant The patient seems to be in fairly good general health

The plantar surfaces of the feet, and particularly of the heels, showed pronounced hyperkeratosis The dorsal surfaces of the feet and toes were slightly scaly and mildly erythematous The palms were dry and scaly and showed accentuation of the natural lines The backs of the hands and fingers were similarly affected, but to a lower degree The anterior and lateral aspects of the thighs and hips showed erythema, scaling, wrinkling and mottled hyperpigmentation The

3 0 cm One on the dorsum of the tongue was white on top, suggesting a secondary leukoplakic reaction The rest of the oral cavity was free of lesions

DR B J KENNEDY, Boston (by invitation) The woman was given urethane because of reports describing its use in leukemia and a few isolated carcinomas Urethane is called ethyl carbamate and is an ancient anesthetic for animals Haddon and Sexton (Influence of Urethane on Experimental Tumors, *Nature,* London **500** 157, 1946) found that phenyl carbamate and phenylurethane produced regression of mammary carcinoma in mice and Walker carcinoma in rats This led to investigation with urethane which produced the greatest effect, especially in the carcinomas There were scarring and decrease in the mitoses in the cells Another group from the same hospital began using urethane in human beings (Paterson, E , Haddow, A , Ap Thomas, I , and Watkinson, J M *Lancet* **1** 677, 1946) They tried it in 19 patients with myeloid leukemia, 13 with lymphatic leukemia and 13 with various types of carcinoma Among the last group only 4 (including patients with Hodgkin's disease and a salivary gland carcinoma) showed some regression of the tumor while the others had but little response The reaction in the patients with myeloid leukemia was striking In nineteen to forty-seven days the urethane produced a reduction in the white cell count of 20,000 or more cells It was found that this reduction of the white cells was chiefly in the neutrophils The hemoglobin did not seem to be affected, or the red cell count, and when the patients were given 100 Gm or more of the drug the hemoglobin rose an average of 27 per cent The patients with lymphatic leukemia showed a similar response but not as striking as did those with myeloid leukemia It was concluded that the urethane treatment of leukemia may be comparable to roentgen therapy The rise in hemoglobin, decrease in white cell count and reappearance of normal differential counts all followed the same pattern as would be expected with roentgen treatment Because of this and the close relation of mycosis fungoides to lymphomatous disease, urethane was given to this patient My co-workers and I plan to give it to a large series of patients to determine whether or not it is a drug that should be used in these cases This patient has been treated for almost two weeks, and the only response so far is perhaps some drying of the skin

DR JACOB H SWARTZ Have you read any reports citing granulocytopenia as a complication of this treatment?

DR B J KENNEDY, Boston (by invitation) Leukopenia develops in many of the patients If this reaction occurs, the drug must be withdrawn I have not heard of the occurrence of granulocytopenia

DR ARTHUR M SIMMONS What is the method of administration and dosage?

DR B J KENNEDY, Boston (by invitation) It is given orally, 1 Gm four times a day At present I do not believe that there is any definite dose that one can adhere to, we expect to try to increase the amount

Extensive Nevus Pilosus et Pigmentosus (von Recklinghausen's Disease?) Presented by DR G MARSHALL CRAWFORD, Boston

A Case for Diagnosis (Lupus Erythematosus? Tuberculosis Luposa?) Presented by DR ROBERT H GOLDFARB, Boston

Telangiectasia, Essential, Limited to Calves Presented by DR MAURICE M TOLMAN, Boston

C B , a 32 year old white housewife, is shown with changes on the backs of her legs which have been present for three and one-half years The patient first

region of the hypochondria and the under surfaces of the breasts showed a definite picture of poikiloderma, consisting of reticulated pigmentation, telangiectasia and atrophy There was decided wrinkling of the upper parts of the breasts and reticulated hyperpigmentation and atrophy in both axillas The lower part of the back, inner aspect of the upper extremities and back of the neck were scaly and erythematous The axillary lymph glands were enlarged The upper eyelids showed erythema and edema, which had been present for the past two months

Laboratory examinations, including urinalysis, serologic tests of the blood for syphilis and complete and differential blood counts, gave essentially normal results

Biopsies of material taken from the skin under the breast and from the thigh showed features of poikiloderma

DISCUSSION

Dr Nathan Sobel The patient definitely had poikiloderma in the areas over the lower part of the breasts and atrophy over extensive areas elsewhere, but I am puzzled by the hyperkeratosis of the palms and soles and do not believe that is often found in cases of poikiloderma

Dr E W Abramowitz I have the same difficulty in reconciling the hyperkeratosis of the palms and soles I do not recall having seen it in cases of poikiloderma It is a question whether some other disease should be considered or whether further observation is necessary before the case is labeled poikiloderma

Dr George C Andrews The case reminded me of the cases of dyspituitarism with poikiloderma-like changes, reported by Bruno Bloch I think that the woman has endocrine disease A basal metabolism test, roentgenograms of the sella turcica, an encephalogram and various other tests are indicated In many cases of Cushing's basophilism the disease is related not to the pituitary but to the adrenal glands, so this case should be studied from that angle I am wondering whether the hyperkeratosis of the soles could be related to localized myxedema in which there is a great deal of lymph stasis that produces verrucous changes

Dr E W Abramowitz Dr Andrews brought up a point which might still point to the pituitary The patient may have keratoderma climactericum

Dr Fred Wise I agree with those who believe that the eruption is caused by a polyglandular disturbance similar to Cushing's syndrome, in which almost invariably telangiectasia and pigmentation of the lower portion of the breasts are present Poikiloderma is merely a symptom, whereas poikiloderma vasculare atrophicans is a definite clinical entity, as described by Jacobi This patient has a poikilodermatous skin associated with polyglandular disturbances, but the condition should not be described as a case of Jacobi's disease because, as the name suggests, that has a variegated appearance It would be better to describe it under a name which at least suggests pituitary basophilism or Cushing's syndrome

Dr David Bloom I realize the difficulty in diagnosing this condition Besides the poikiloderma-like eruption and the scaly plaques, the patient shows extensive keratosis of the palms and soles, which would fit in with psoriasis or keratoderma climactericum One finds erythema of the eyelids in poikilodermatomyositis, but in this patient it developed only one month ago, late in the course of the disease I am inclined to agree with Dr Andrews and Dr Wise in regard to a thorough study of the patient in order to eliminate an endocrine condition such as Cushing's pituitary basophilism A definite diagnosis, of course, cannot be made at present

A Case for Diagnosis (Leukonychia and Hyperpigmentation of Gums and Lips) Presented by Dr E W Abramowitz

noted these lesions on both her thighs and her legs Those on the thighs have gradually cleared, but lesions have persisted on the calves She stated that she bruises too easily but gives no history of epistaxis It was stated that some lesions bled on several occasions following minor trauma This woman was extremely nervous and suffered from melancholia during her only pregnancy five years ago, she has taken sedatives at night since that time There has been considerable menstrual irregularity The general medical history was otherwise noncontributory There was no history of similar lesions or of epistaxis in the family

Examination revealed a profusion of dilated blood vessels restricted to the lower third of each calf Most of these are of telangiectatic caliber but some are slightly larger They gradually fade out on the middle portion of the calves and on the sides of the legs

The prothrombin time (clotting time) of the blood plasma was found to be 20 seconds The sedimentation rate of the blood was 3 mm in 1 hour The cellular elements of the blood were normal A specimen removed for histologic examination revealed only atrophy of the epidermis and fibrosis of the corium One small area was treated by electrodesiccation with some resultant diminution in telangiectasia

DISCUSSION

DR WALTER F LEVER This disorder is really not too rare It was first described in the American literature by Stokes (*Am J M Sc* **149** 669, 1915) under the name of generalized telangiectasia and was thought to be associated with syphilis Among subsequently reported cases some patients had syphilis, but in most instances they did not It was also found that the disorder was not necessarily generalized, in patients with localized distribution the lower legs are most commonly affected The telangiectatic vessels are dilated venules They are dilated because their innervation is defunct Recently, in a patient with telangiectasia of the lower legs, I injected both a vasoconstricting and a vasodilatory drug intradermally, following Perutz' directions (*Arch f Dermat u Syph* **148** 313, 1924-1925) Intradermal injection of 0 1 cc of a 10 per cent solution of caffeine sodium benzoate caused the skin around the site of injection to become bright red, but the affected vessels did not change their size Similarly, 0 1 cc of a 1 1,000,000 solution of epinephrine injected intradermally caused blanching of the skin around the site of injection, but did not affect the telangiectatic vessels The disorder is harmless as such, but it is advisable to examine such patients for syphilis

Lichen Striatus in a 4 Year Old Girl Presented by DR G MARSHALL CRAWFORD and (by invitation) DR J H COX, Boston

Bernard Appel, M D, *President*

G Marshall Crawford, M D, *Secretary*

April 9, 1947

Psoriasis (Mycosis Fungoides?) Presented by DR JACOB H SWARTZ, Boston

Keratoses, Due to Arsenic, Taken for Psoriasis Presented by DR EDWARD A LAFRENIERE, Arlington, Mass

DISCUSSION

DR F RONCHESE, Providence, R I I wonder whether anybody here has treated keratoses with ozonides This treatment was reported by Sharlit (New

Maurice J Costello, M D, *President*

Wilbert Sachs, M D, *Secretary*

Oct 14, 1947

Generalized Progressive Scleroderma and Dermatomyositis Improved with Diphenhydramine (Benadryl®) Presented by Dr Maurice J Costello

J F, a married woman aged 42, was presented before this Society on Oct 10, 1944, with a generalized progressive scleroderma and dermatomyositis associated with acrosclerosis and Raynaud's phenomenon

Since March 1946 she has been given 400 mg of diphenhydramine daily, with remarkable improvement, there is increased mobility of the joints and softening of the boardlike infiltrations and the dyspnea, wheezing, dysphagia and loss of muscle power have been relieved to a remarkable extent The results have been so spectacular that the only abnormality remaining is the irreversible contraction of the fourth and fifth fingers

DISCUSSION

Dr David Bloom I believe that diphenhydramine in such large doses should be given to a patient only when he is hospitalized and under close observation I saw a patient who had received 150 mg of the drug daily over a period of several weeks suddenly collapse with a sensation of constriction in the chest and numbness of the upper extremities

Dr Maurice J Costello The patient's condition was so advanced that she had not only severe edematous thickening of the skin and lack of mobility of the joints but also dysphagia and dyspnea Her general practitioner gave her diphenhydramine mainly to relieve what he considered asthmatic symptoms, and she has taken 400 mg every day for a year and a half I presented this patient before this society in 1944, and the change since has been nothing short of remarkable This patient had received dihydrotachysterol (hytacherol®) with no benefit

Dr Samuel M Peck When dihydrotachysterol works, it is only on the edematous part If diphenhydramine works, it is something entirely different I think that I shall try iontophoresis with pyribenzamine,® as I am doing with neurodermatitis, especially of the hands I know that the drug stays in the tissues for weeks

Dr Anthony C Cipollaro Does diphenhydramine produce vasodilatation?

Dr Maurice J Costello I believe so, because the patient has been free of the blanching of the fingers associated with Raynaud's phenomena I might add that the only other case I have seen recently that approaches this in therapeutic result was that of a patient whom I sent from Lenox Hill Hospital to Bellevue Hospital, who received a high protein diet with large doses of a protein hydrolysate (amigen®) Graphic studies were taken of the improved mobility of the joints and the skin overlying them

Dr Samuel M Peck Was there a reversal of result with primary lesions again with a violet ring?

Dr Maurice J Costello No I have never seen improvement from dihydrotachysterol that was permanent The diphenhydramine was discontinued in this case for three weeks, with recurrence of symptoms

York State J Med 46 2147 [Oct 1] 1946) who used with success in dyskeratotic dermatoses triolein ozonide, which is formed in olive oil on ozonization

DR NEVILLE KIRSCH, Hartford, Conn (by invitation) Sharlit has used ozonides in oil By rubbing in the oil four times daily his patients succeeded in eliminating keratotic lesions It has also been employed by MacKee The product may be obtained from G F Harvey & Company of Saratoga Springs, N Y, and must be refrigerated Twenty per cent of the ozonide mixture is incorporated in an appropriate base and rubbed in four times a day for six to eight weeks

DR WALTER F LEVER, Boston I have had no experience with ozonides, but I suggest treatment with 2,3-dimercaptopropanol (BAL) Since in this patient the arsenic preparation was given only two years ago, there may still be some arsenic remaining in her tissues, and it might continue to form keratoses BAL is effective in liberating organic arsenic from tissue

Dermatitis Herpetiformis (Contact Dermatitis from Rubber?) Presented by DR CARL A DAHLEN, Boston

T B, a 23 year old white girl, displayed an eruption of two years' duration, affecting the forearms, scalp, trunk and buttocks The first lesions appeared on the forearms in the form of vesicles At some later date the scalp became affected Lesions developed on the back and buttocks about a year ago Itching and burning have been severe, the patient claimed to be exhausted at times from these symptoms

On examination this young woman revealed a symmetric eruption affecting the scalp, forehead, elbows, dorsal aspects of the forearms, shoulders, scapular areas, lower part of the trunk and buttocks On the back is a transverse band of clear skin at the level between the brassiere and girdle areas The primary lesions are grouped vesicles and papules with crusted excoriations and pigmented scars These changes are most pronounced on the elbows, shoulders and hips The lines demarcating the clear zone across the back are rather sharp Both the upper part of the back and the girdle area below reveal a mild diffuse erythema, and there is a minimal amount of fine branny scaling on these regions On the upper part of the back there are three moderately distinct rectangular patches, which stand out from the previously defined changes One is seated transversely across the middle part of the back, the other two are vertically parallel to each other on the midscapular regions These patches are approximately 5 by 15 cm in size and display a perceptible thickening with more scaling than the surrounding skin

Results of an examination of the urine and a hemogram were normal Treatment included use of diphenhydramine hydrochloride (benadryl®) 0 05 Gm three times daily for five weeks, followed by sulfapyridine, 0 5 Gm, twice daily for two weeks Two suberythema doses of ultraviolet rays were given prior to the sulfonamide drugs There had been temporary improvement from these measures

DISCUSSION

DR FRANCIS M THURMON, Boston I agree with the diagnosis of dermatitis herpetiformis If sulfapyridine were used in larger dosage, it would be more effective

DR GEORGE SCHWARTZ, Boston I disagree This is contact dermatitis due to rubber inserts in her brassiere and girdle I had the patient put on her girdle, and the lower portion of the eruption formed a complete outline of the garment The dermatitis is now becoming generalized

A Case for Diagnosis (Lymphatic Leukemia Following Vaccination Against Smallpox?) Presented by DR DAVID BLOOM

J H, a man aged 80, was referred to me in September 1947 by Dr H Wolf because of a tumor which had developed in the area of smallpox vaccination five months previously The patient also suffers from generalized pruritus

On the external aspect of the right arm there was a walnut-sized, erythematous, raised and indurated, globular tumor, firm in consistency and with borders infiltrating the surrounding skin in an ill defined manner In the vicinity of the tumor there were a number of erythematous, pea-sized and excoriated papules In addition to this lesion which caused severe pruritus, there were excoriated lesions on the forearms, the lumbosacral region and the legs In the axillas slightly enlarged nodes were palpable

Biopsy of the tumor on the arm revealed a "nonspecific type of granuloma" A blood count on two occasions showed a normal red cell count, but a white cell count of 13,600 on one occasion and 16,900 on another The differential count, in addition to 3 per cent blasts, showed 58 per cent lymphocytes and 35 per cent polymorphonuclear leukocytes and on another occasion 76 per cent lymphocytes

The patient is in good general health except for the generalized pruritus which disturbs his sleep The lesion on the right arm has diminished in size after several treatments with filtered roentgen rays

DISCUSSION

DR WILBERT SACHS The microscopic section that I examined was from the arm and suggested a nonspecific granuloma The characteristic picture of lymphatic leukemia, which undoubtedly should be present in a lesion of this size, was not seen If the patient has lymphatic leukemia, it is unrelated to the lesion on the arm

DR SAMUEL M PECK A number of years ago I thought that it would be interesting to take cases of chronic lymphatic leukemia, acute leukemia and diseases like purpura hemorrhagica and do trichophytin, tuberculin and venom tests and study the histologic appearance, to see how a known blood picture would influence a histologic reaction with which I was familiar I found nothing very striking

DR WILBERT SACHS Instead of a leukemia infiltration, one finds a leukemid type of reaction, and this is nonspecific

DR ANTHONY C CIPOLLARO Does the patient have leukemia in the first place, and did vaccination have anything to do with it if he has? There has not been enough evidence to indicate a relation between smallpox vaccination and leukemia

DR DAVID BLOOM The diagnosis of leukemia was suggested by the increase in the white blood cells, the high lymphocyte count and the presence of blasts This opinion was shared by the hematologist, who advised sternal puncture In spite of the absence of a confirmatory histologic report, this diagnosis is most probably correct

Acrodermatitis Pustulosa Perstans Presented by DR WILBERT SACHS

Lymphoblastoma, Clinically Poikiloderma, Histologically Mycosis Fungoides Presented by DR JACK WOLF

DR WALTER F LEVER, Boston That would not explain the lesions on the forehead and scalp I agree with the presenter's diagnosis of dermatitis herpetiformis and would suggest that sulfapyridine be given in larger amounts I have observed a case in which there was no response until 6 Gm a day were given The patient has been taking that dose for six months, and it controls the eruption

DR JOSEPH GOODMAN, Boston What blood level of sulfapyridine was reached with that amount?

DR WALTER F LEVER, Boston I have done no determinations of the blood level

DR WILLIAM P BOARDMAN, Boston The patient told me that she was just as uncomfortable while taking sulfapyridine If the sulfonamide drugs are not well tolerated or are ineffective, why not try potassium arsenite solution (Fowler's solution) which has long been known to be effective in dermatitis herpetiformis?

DR JOSEPH GOODMAN, Boston The use of sulfapyridine in dermatitis herpetiformis interested me in relation to a patient I treated recently, starting as Dr Lever did and increasing to a maximum dose of 6 Gm a day My patient had typical dermatitis herpetiformis The drug was given in gradually increasing amounts over a period of three months At the end of that time she took 6 Gm daily for two and one-half weeks The blood level was slightly over 7 mg per hundred cubic centimeters, an adequate level of sulfapyridine The dermatitis did not improve more than 20 per cent It was a question whether 8 Gm a day would be effective The blood level seemed adequate, and I was a little uneasy about the situation as it was I wonder how many failures with sulfapyridine have been seen by the members of this society, with doses of 3 to 5 Gm daily as a maximum

DR OSCAR GILJE, Oslo, Norway (by invitation) I would like to hear about the treatment of dermatitis herpetiformis with diphenhydramine hydrochloride (benadryl®) Two patients in Norway whom I treated with benadryl® were relieved In 1 of the cases the disease was of six years' duration and in the other one-half year When benadryl® therapy was stopped, the itching became worse, the patients improved on resuming treatment with benadryl®

DR BERNARD APPEL, Lynn, Mass I questioned this patient about her reaction to benadryl® and she told me that it did not help her pruritus It did procure a good night's sleep and made her feel more relaxed but apparently did not relieve the itching I would agree with the diagnosis of dermatitis venenata due to rubber in the clothing The entire picture is consistent with that diagnosis, not only because of the definite, clear, smooth, symmetric pattern which corresponds to the articles of clothing worn that contain rubber but also because the rest of the eruption is consistent with it Contact dermatitis due to rubber from articles of clothing may produce generalized eruptions The presence of vesicles certainly does not contradict the diagnosis of contact dermatitis

DR JACOB H SWARTZ, Boston How often do you see clusters of scars in dermatitis from rubber?

DR BERNARD APPEL, Lynn, Mass Consequent reactions like crusting, follicular involvement, pigmentation and all the so-called "id" type of lesions depend, first, on the duration and, second, on the particular patient's sensitivity and intensity of reaction

A Case for Diagnosis (Lichen Planus? Psoriasis?) Presented by Dr Nathan Sobel

G F, a woman aged 52, was first seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Oct 16, 1947 with an eruption of six weeks' duration

On the right upper eyelid there is a well defined, oval plaque which shows an erythematous, raised border and depressed, crusted center On the buccal mucosa there are divided plaques with reddish borders The entire scalp shows thickening of the skin, erythema and scaling There are erythematous, superficial, slightly scaly, well defined round plaques on the chest and on the upper part of the back and arms on the left On the extensor aspect of the thighs and inner aspect of the right thigh there are some purplish lichenified plaques There are erythema and fissuring in the genitocrural creases All the finger nails show onycholysis The nails of both big toes are greatly discolored, thickened and loose

The only laboratory report available to date is on the Wassermann reaction of the blood, which was negative

DISCUSSION

Dr David Bloom The patient presents lesions on the lower extremities and on the buccal mucosa which look like lichen planus and an eruption of the scalp and changes in the nails suggesting psoriasis This combination of psoriasis and lichen planus has been reported on several occasions

Dr Nathan Sobel I think that the lesion on the left buccal mucosa is probably a bullous lesion of lichen planus I have also previously seen lichen planus on the scalp To settle the question, biopsy would be necessary I think the changes in the nails are psoriatic

Note.—It was reported at the succeeding meeting, in November, that biopsies, one from the leg and another from the neck adjacent to the scalp, both showed mycosis fungoides

A Case for Diagnosis (Peculiar Eruption of Granuloma Annulare?) Presented by Dr David Bloom

M McH, a woman aged 41, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in October 1947, complaining of an eruption of one year's duration The eruption started first on the elbows, later it appeared on the lower extremities, and in the past three months it has involved the wrists There are no subjective symptoms

On the posterior and internal aspects of both lower extremities, extending as far as the middle of the legs, there is a profuse eruption of bluish-brownish, flat lesions, from the size of a lentil to that of a pea, some of which feel somewhat infiltrated A similar but less profuse eruption is seen on the flexor and internal aspects of both upper extremities Over both knees and elbows there are pink to skin-colored, raised, indurated papules Similar lesions are seen over the external malleolus of the left leg There are a moderate number of raised, dark red, firm, globular and elongated lesions on the flexor aspect of both wrists, extending to the forearm Over the sacrum, similar lesions form an irregularly shaped plaque

Microscopic examination of lesions from the wrist, elbow and thigh all showed the structure of granuloma annulare As reported by Dr Charles F Sims, the epidermis was thin, and the corium beneath showed basophilic degeneration In the upper and middle parts of the cutis were areas of granular degeneration surrounded by small, round and wandering connective tissue cells, epithelioid and giant cells The infiltrate took an arciform arrangement in many areas

DR JOSEPH GOODMAN, Boston I think that we are going far afield when we call this a contact dermatitis Let us assume, with Dr Schwartz, that this eruption corresponds exactly to the rubberized areas of the girdle It has spread to the forehead, scalp and elbows In contact dermatitis severe enough to produce a widespread eruption one must also expect a local extension I cannot conceive of a dermatitis of this sort spreading so widely without becoming generalized on the trunk I am sure that if these lesions were not in the area touched by her girdle, there would be no doubt about dermatitis herpetiformis

DR JOHN G DOWNING, Boston Two months ago this girl presented a classic picture of dermatitis herpetiformis, with the characteristic symptom of burning She showed grouping, pigmentation and atrophic scarring Today there is unquestionably a superimposed contact dermatitis which might be due to the elastic in the straps of her brassiere

DR CARL A DAHLEN, Boston There was considerable relief from treatment with benadryl,® but the patient failed to return The next time we saw her she had a recurrence I decided to give sulfapyridine, and it was prescribed in a dose of 0 5 Gm twice a day, but she still did not report back as instructed If she were cooperative, I might have obtained better results by increasing the sulfapyridine

DR FRANCIS P MCCARTHY, Boston This girl had a very interesting tongue She showed linear filiform papillae along the margins and beneath these areas were tufts of white hairlike papillae I made a diagnosis of depigmented congenital defect of the filiform papillae Some textbooks indicate that there are oral lesions in dermatitis herpetiformis I have never observed them, although I have been searching for years Has anyone here seen lesions in the mouth in dermatitis herpetiformis?

DR FRANCIS M THURMON, Boston I have seen 2 cases, one was shown to me in Chicago and the other was presented by me at a meeting of this Society

DR WALTER F LEVER, Boston I have seen 1 patient His eruption responded well to the usual doses of sulfapyridine, 2 to 3 Gm a day There was no doubt about the diagnosis

Lichen Planus of the Eyelids and Buccal Mucous Membranes Presented by DR WILLIAM J MACDONALD, Boston

Lichen Sclerosus et Atrophicus (Generalized) Presented by DR JOSEPH GOODMAN, Boston

DISCUSSION

DR JOSEPH GOODMAN, Boston This 43 year old woman has been followed in the clinic for six months At the start there was a hyperkeratotic follicular eruption characterized by small horny spicules She had alopecia when first seen, and this has extended since then It was thought at first that this was a vitamin A deficiency, but the vitamin A level and carotene level were normal In spite of that she received 200,000 units of vitamin A daily for a period of two months, during which time the eruption became worse The patient was then admitted to the hospital, and a biopsy was performed on the scalp lesions Those on the arms began to look like lichen planus and others have too, but at the same time many of the horny spicules seen when she was first observed in the clinic have persisted The picture presented today corresponds closely to the description of the disease called "lichen planopilaris" by Sachs and De Oreo (ARCH DERMAT & SYPH **45** 1081 [June] 1942)

DR WILBERT SACHS I should consider other possibilities in preference to granuloma annulare Before accepting this diagnosis, I should like to study the microscopic sections Although numerous giant cells may be found as a rule they are not a feature of granuloma annulare

DISCUSSION

DR THOMAS N GRAHAM I think that the individual papules on the dorsum of the right hand look like the lesions usually observed in granuloma annulare, although they are not in annular formation However, the lesions on the forearm do not resemble that dermatosis clinically but, rather, suggest lichen planus

DR FRANK E CORMIA (by invitation) Dr Peck and I had the same opinion—that, clinically at least, the lesions are suggestive of amyloidosis

DR SAMUEL M PECK What struck me was the two distinct types of lesions The first was the skin-colored lesions on the back of the hands and even on the elbows which I should not hesitate to call granuloma annulare Then I saw another type, peculiar brownish-bluish lesions which made me think of amyloid disease but the fact that the microscopic appearance of three lesions was the same makes me doubt that we are dealing with amyloidosis The peculiar cases shown at the meeting of the American Academy of Dermatology and Syphilology in Chicago turned out to be extracellular cholesterosis I should certainly like to see studies made along that line

DR ISADORE ROSEN The clinical features suggest the lichenoid type of sarcoid rather than granuloma annulare

DR NATHAN SOBEL One of the thoughts that first occurred to me was possible amyloidosis, but against that is the complete absence of itching, which is certainly a distinctive feature of amyloidosis The lesions around the anterior surface of the wrist are skin colored and hard and could fit into the picture of granuloma annulare The other lesions are not characteristic and look almost like lichen planus at a casual glance I think it best to include all the lesions as granuloma annulare

DR MAURICE J COSTELLO This case impressed me also as one of lichenoid sarcoid I should like to see the results of tuberculin tests and roentgen examination of the chest I think that it is true that granuloma annulare responds to roentgen rays

DR DAVID BLOOM The biopsy report was surprising to all of us who had observed this case and did not think of the diagnosis of granuloma annulare Although I have seen atypical cases on several occasions, particularly of disseminated granuloma annulare in children, I have never seen a case similar to this one The patient will be studied more thoroughly

Darier's Disease Presented by DR NATHAN SOBEL

A Case for Diagnosis (Keratoses? Lupus Erythematosus?) Presented by DR ANTHONY C CIPOLLARO

Mycosis Fungoides Presented by DR MAX SCHEER

Parapsoriasis Guttata Presented by DR MAX SCHEER

Hypersensitivity to Cinnabar in a Tattoo Presented by DR JACK WOLF

Multiple Superficial Basal Cell Epithelioma with Arsenical Keratoses Presented by DR JACK WOLF

Multiple Epidermal Cysts of the Skin Presented by DR F RONCHESE, Providence, R I

A 14 year old white school girl, G deB , American-born of Portuguese parents, is presented with lesions which have been present on her face since birth They have not been observed to change appreciably with the passage of time She had



Fig 1—Multiple epidermal cysts of the skin The face of a 14 year old girl studded with milia, a few isolated lesions of keratosis pilaris and erythema

no hair anywhere until the age of 3 years, at that time a little began to appear on her scalp, and it developed slowly thereafter There were no eyebrows until the past few years, and no hair has developed elsewhere The patient has always been in good health There is no history of similar disturbances among other members of the family Negro ancestry was denied The patient seemed of normal intellect and was progressing well at school

NEW ENGLAND DERMATOLOGICAL SOCIETY

Bernard Appel, M D, President

G Marshall Crawford, M D, Secretary

Boston, Feb 12, 1947

Incontinentia Pigmenti Presented by DR G MARSHALL CRAWFORD, Boston, and DR C R DAMIANI, Worcester, Mass

A 4 year old white girl of American birth, P W, is presented with an eruption on the trunk and upper part of the thighs present since early infancy At about the age of 3 months, pigmented streaks were seen on the back of the upper part of the thighs These gradually became more pronounced and extended upward, eventually involving the back and abdomen A year ago, when the patient had measles, the pigmented areas were observed to become scarlet, after recovery the areas gradually returned to the previous shade of brown No other member of the family has been affected by any similar condition There was no history of congenital anomalies, the child had a normal developmental history and was mentally alert

Examination reveals a pigmentary disturbance approximating the "bathing suit" distribution The upper limits are the xiphoid level anteriorly, the axillas laterally and the inferior edges of the scapulas on the back It extends downward over the trunk and across the hips and buttocks to about the junction of the upper and middle thirds of the thighs The lesions consist of symmetrically arranged striate and whorl-like pigmentary deposits of medium brown The majority of them are linear, and their length varies from 1 to 3 cm, most lesions are from 3 to 5 mm in width They are arranged in parallel fashion corresponding roughly to the cleavage lines of the metameric segments

A biopsy was performed, and histologic observations were reported as "consistent with lentigo"

DISCUSSION

DR WALTER F LEVER The histologic picture bears out the diagnosis of incontinentia pigmenti Considerable amounts of melanin were present in the upper part of the corium, whereas melanin in the basal layer was not increased Other forms of hyperpigmentation usually show increased pigmentation both in the basal layer and in the upper part of the corium

DR WILLIAM R HILL I think that Sulzberger and Bloch reported a case of incontinentia pigmenti and concluded that it was a familial disorder This case is not familial

DR WALTER F LEVER In several of the reported cases other abnormalities, such as ectodermal defects, were present in the patient as well as in members of the patient's family There is, however, only one report, that of Naegeli (cited by Sulzberger, M B, ARCH DERMAT & SYPH **38** 57, 1938), concerning the familial occurrence of incontinentia pigmenti Thus, the absence of a familial history is not against incontinentia pigmenti

There is a luxuriant growth of kinky hair on the scalp and the facial conformation is Negroid The face is reddish pink The skin thereon appears granular and feels slightly rough It is entirely covered with densely packed miliary lesions of 0 5 to 1 0 mm diameter, these are pearly white and smooth Diascopic examination shows complete blanching of the lesions No telangiectases can be observed The patient's eyebrows are sparse, scaly and also studded with milia The remainder of her skin exhibits no hair The lateral aspects of the arms and thighs reveal a sparse eruption consistent with keratosis pilaris, and a few isolated lesions on the face are similar in type No scars can be found anywhere

The Hinton reaction of the blood was negative Results of examination of the urine were normal A hemogram was normal with the exception of a leukocyte

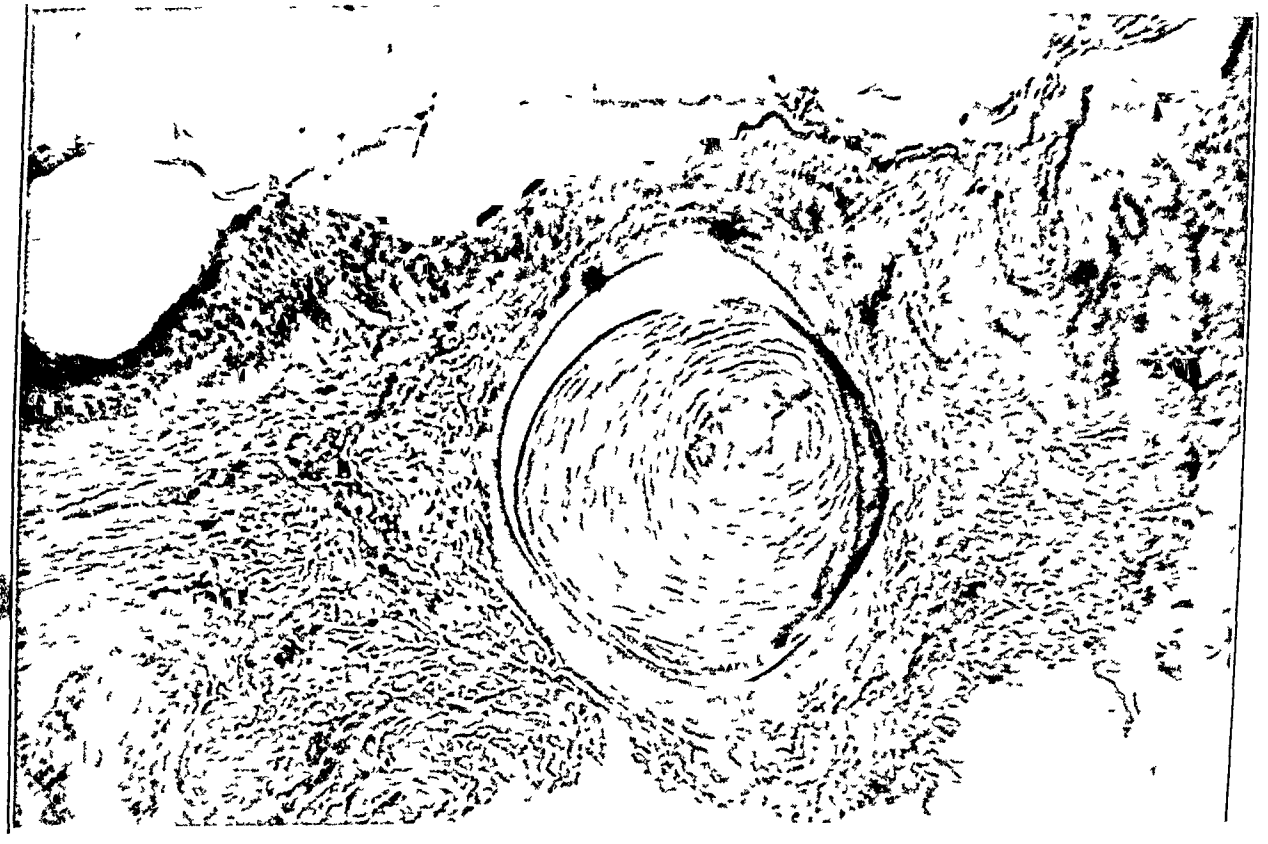


Fig 2—Multiple epidermal cysts of the skin Histologic section showing epithelial cysts

count of 10,750 cells per cubic millimeter The nonprotein nitrogen and glucose content of the blood were normal Histologic examination of a biopsy specimen revealed a moderate degree of hyperkeratosis There were cystic cavities about 0 2 mm in diameter just beneath the epithelium, these were lined with squamous epithelium and filled with a laminated keratotic mass No treatment had been administered until the past two months, during which time the patient has taken 200,000 units of vitamin A daily, there has been no appreciable improvement

DISCUSSION

Dr Jacob H Swartz, Boston Although I am in accord with Dr Ronchese's diagnosis, I should like to point out that the patient had definite hyperkeratotic

DISCUSSION

DR S J ZAKON The internists recognize this as part of the signs and symptoms of the Chvostek Habitus (Chvostek, F Cirrohis of the Liver, *Wien Klin Wchnschr* **35** 381, 1922), in which there are ascites and jaundice, pulsating spider nevi and loss of body, axillary and pubic hair This is usually observed in nonobstructive jaundice

DR HAMILTON MONTGOMERY, Rochester, Minn My co-workers and I have seen a number of pulsating hemangiomas of the skin in patients referred by various internists in our clinic Dr Williams and Dr Snall reported a series of these cases (*Arch Int Med* **62** 872-882 [Nov] 1938) All the phenomena that have just been mentioned are not necessarily present Pulsating hemangiomas are almost invariably associated with cirrhosis of the liver

DR THEODORE CORNBLEET At the Cook County Hospital various clinicians have pointed out for years that there is a lack or sparsity of hair about the male abdomen and chest in the presence of cirrhosis of the liver My associates and I always suspect that there is cirrhosis of the liver in such cases In a number of these patients telangiectases of the chest and upper part of the abdomen and a few of the blood vessel enlargements can be seen, or more often felt, to pulsate We have tried the newer nutritional remedies for cirrhosis of the liver, such as methionine and cysteine Though some of those patients were said to be improved clinically and show better results in tests of hepatic function, I have never seen these angiomas and telangiectases disappear thereby I have seen these lesions regress, however, after parturition There is no doubt that in other cases they may clear spontaneously

A Case for Diagnosis (Lupus Erythematosus, Telangiectatic Type?) Presented by DR CLEVELAND WHITE and (by invitation) DR J L MADURA

Squamous Cell Carcinoma of the Penis Presented by DR M OPPENHEIM and DR D COHEN

Mr C P, a Negro aged 49, has a tumor-like lesion on the penis of four years' duration There is no pain but some tenderness on pressure The lesion is about the size of a half-dollar and is situated on the outside of the prepuce It has an irregular configuration, in some places polycyclic with overhanging margins There are yellowish crusts and scales on the surface When these are removed, pressure on the tumor cause white millet-sized drops to appear The lesion is indurated and of a cartilaginous consistency There is no inflammation Inguinal glands are not enlarged

On the glans penis there are depigmented, depressed, irregular scars with a smooth flat base and a slight hyperpigmentation in the periphery This lesion began as a solid nodule four years ago (1943) and has progressed until the present time In 1943 and in 1917 the patient received treatment for his blood For many years he was a laborer on a railroad, and now he is employed in an ice cream factory. No history of exposure to oil is given

The urine is normal The blood cell count is normal The Kahn reaction of the blood was negative on April 19, 1947, and on April 20, 1947

Biopsy of the skin reveals acanthosis, mainly limited to the large rete projections The prickle cell layer is growing atypically Little mitosis is present There is a dense lymphocytic infiltration in the dendritic ramifications of the papillary layer

DISCUSSION

DR S J ZAKON About two weeks ago I saw a man with carcinoma of the penis which had been treated for syphilis for some time I reviewed the literature, which is mostly in the field of urology (Melicow, M M, and Ganem, E J Cancerous and Precancerous Lesions of the Penis, *J of Urol* **55** 486, 1946) Early diagnosis is advised because of the serious prognosis It is interesting that there has never been a report of a case of carcinoma of the penis in a Jew, not because of any racial immunity but because of early circumcision In the Mohammedans, who circumcise their children at the age of 13, there is a definite incidence of carcinoma of the penis With early diagnosis some patients will recover In the far advanced case, even with radical amputation and removal of the regional glands, the prognosis is poor

DR THEODORE CORNBLETT In a recent communication of *Science* (**105** 391 [April 11] 1947), Plant and Kahn-Speyer mention that carcinoma of the penis does not occur in persons who have been circumcised in the first few weeks of life and is rare in those who have been circumcised in childhood or in early puberty This induced them to study the carcinogenic action of smegma in mice using material obtained from horses Their work was evidently done carefully with suitable controls and showed that smegma is carcinogenic

This man's lesion was not highly characteristic for carcinoma of the penis, though that diagnosis is probably correct Epitheliomas at this site are usually of the squamous cell type and highly malignant Yet the present lesion began four years ago and the regional lymph glands are not enlarged

DR HAMILTON MONTGOMERY, Rochester, Minn I do not believe that this is an epithelioma histologically There are well defined pearls but few mitotic figures The cells are edematous and large, and there is an area of parakeratosis I think that this is a condyloma acuminatum and not an epithelioma As brought out by the first discusser, epithelioma of the penis usually grows rapidly except those that start on the foreskin In cases in which there is a so-called precancerous stage, moist leukoplakia or erythroplasia, simple circumcision is often enough to prevent the lesion from becoming a frank epithelioma I do not believe that in this patient amputation of the penis will be necessary

DR STURE JOHNSON, Madison, Wis (by invitation) I wonder whether the disease might be histoplasmosis At Ann Arbor, Mich, I saw 2 patients with lesions of histoplasmosis of the genitalia By careful search my co-workers and I were able to demonstrate the organisms in the tissues Schaeffer and his group have also reported cases in which the lesions were present on the genitalia Genital involvement with Histoplasma capsulatum is not unusual The organisms are usually difficult to detect in tissue and to culture I should like to call attention to two articles with photographs of genital histoplasmosis one by Palmer, Almolsch and Shaffer (ARCH DERMAT & SYPH **45** 919 [May] 1942) and the other by Curtis and Cawley (*J Urol* **57** 781 [April] 1947)

DR MAURICE OPPENHEIM (by invitation) The site of this epithelioma is unusual It is not the favorite place The favorite site for carcinoma of the penis is on the inside and on the glans The striking thing is that it has taken four years for it to grow to this size

I do not agree with Dr Montgomery that the histologic observations are atypical with few mitotic figures There is a decided inflammatory reaction surrounding the atypical epithelial growth This carcinoma looks like the so-called mule-spinner cancer, which is produced by lubrication oil used in cotton mills in England and Scotland

follicular lesions on her forehead and similar changes on other areas where one finds Darier's disease I would suggest watching for the development of more evidence of keratosis follicularis

DR F RONCHESE, Providence, R I Dr Bernard Appel suggested to me the diagnosis of ulerythema ophriogenes This would be correct for the miliosis and the erythema, but there is no scarring The keratosis pilaris is limited to a few elements and the miliosis-erythematosis is not limited to the eyebrows but extends to the entire face However, this is an excellent suggestion, and an investigation will be made on the relation of this case to that rare entity which has been called ulerythema ophriogenes sive superciliare Tanzer, folliculitis rubra Wilson, keratosis pilaris rubra faciei Brocq and red keratosis pilaris Bazin This case is a good demonstration of the origin of milia in the hair follicle, the lesions eventually becoming keratosis pilaris, to be differentiated from the pseudomilia following epidermolysis bullosa or pemphigus and the miliary calcified sebaceous cysts It could be considered as a nevoid ectodermal defect

A Case for Diagnosis (Sinuses, Nodules and Ulcers of the Buttock Tuberculosis Colliquativa? Actinomycosis?) Presented by DR JACOB H SWARTZ, Boston

DISCUSSION

DR JACOB H SWARTZ, Boston I have two more tentative diagnoses to add symbiotic infection with Staphylococccus and Streptococcus, and dermatitis factitia plus infection I saw this man only once, and no laboratory work was done I will be glad to report on the case at the next meeting

DR FRANCIS M THURMON, Boston I suggest the diagnosis of dermatitis factitia It is asymmetric, and there was one lesion slightly stained, as though something had been applied, there were tiny white vesicles on the top

DR JOHN G DOWNING, Boston For three years I have been treating a man with a similar eruption, which started on his legs after contact with oil I have seen these eruptions on the arms following the same event Cultures from one patient showed that he had a synergistic combination of hemolytic Streptococcus and Staphylococcus

NOTE—A second biopsy specimen was subsequently removed from the patient's thigh, and a sinus tract found in the depth of the wound was curetted to obtain additional material for mycologic study Histologic observations were nonspecific An extemporaneous preparation from curetted material revealed the "sulfur granules" of actinomycosis, and microscopic study showed the characteristic club-shaped formations Cultural studies were confirmatory

Scurvy Presented by DR GEORGE E MORRIS, Boston

E D, a 45 year old white man, formerly occupied as a welder, complained of an eruption on the feet, legs and thighs of six weeks' duration The first lesion appeared on the left thigh as a red scaly patch Three weeks ago the lower extremities rapidly erupted with dark spots all over the legs The patient has consumed considerable quantities of alcohol, and his diet was distinctly inadequate

At this time numerous fading purpuric blotches may be seen on the lower portions of the patient's legs and the dorsa of his feet The remainder of the lower extremities, the buttocks and lower portion of the trunk show a sparse eruption of small, brownish, scaly patches from 0 5 to 1 5 cm in diameter

Dr Francis M Thurmon, *President*

Dr G Marshall Crawford, *Secretary*

Dec 3, 1947

Necrobiosis Lipoidica Diabeticorum Presented by DR MAURICE M TOLMAN, Boston

Basal Cell Epithelioma, of Nose, Forehead, Left Eyebrow and Left Upper Eyelid Presented by DR JOHN G DOWNING and (by invitation) DR HARVEY B ANSELL, Boston

Tinea of Face (Microsporum Fulvum), Neurodermatitis Circumscripta of Wrist Presented by DR SEYMOUR J WHITE, Lawrence, Mass

Chronic Pemphigus of Eye with Cicatrizing Lesions of Skin Presented by DR BERNARD APPEL, Lynn, Mass

Frambesia Tropica (Yaws) Presented by DR JOHN G DOWNING, Boston

E R, an 8 year old Negro girl, has had lesions on the right heel and left gluteal fold for the past ten months The first lesion to develop was on the right sole, it appeared in December 1946 At that time the child resided in Jamaica, British West Indies, where a diagnosis of yaws was made Treatment consisted of one injection of a bismuth preparation and three of arsphenamine, and the lesion healed Another appeared on the right heel in July 1947, and the patient moved to Boston a month later She was first seen in the Boston City Hospital clinic in September 1947, and by that time another lesion had developed in the left gluteal fold There has been good response to therapy

Examination of the right heel when first seen three months ago revealed a raised, crusted, nontender granuloma, 1 5 by 1 5 cm This was surrounded by a 2 cm area of induration and scaling A similar, but smaller, lesion was present in the left gluteal fold but with less induration At this time there is little to be seen on either area The skin is slightly blacker than this moderately dark negroid integument, and a very indistinct trace of induration can be palpated

A dark field examination of material obtained from the lesions revealed organisms indistinguishable from Treponema pallidum The Hinton and Kahn reactions of the blood were positive on two occasions The hemoglobin content and red cell and white cell counts of the blood were normal, a differential smear revealed 48 per cent polymorphonuclear leukocytes, 42 per cent lymphocytes, 8 per cent monocytes and 2 per cent eosinophils Treatment consisted of intramuscular injections of penicillin, a total of 3,350,000 units was administered

Frambesia Tropica (Yaws) Presented by DR JOHN G DOWNING, Boston

D R, a 5 year old Negro boy, a brother of the preceding patient (E R), has lesions on the left heel and the buccal mucous membrane The first change appeared on this little boy's knee after an injury in April 1947 which failed to heal The ulcer was diagnosed as yaws and treated with three injections of a bismuth preparation plus seven of arsphenamine During the time of treatment several other lesions appeared on both legs, but all were healed by the time therapy was terminated He also came to Boston in August 1947 There was no further trouble

The result of the tourniquet test was positive A hemogram was normal, including a count of the thrombocytes The patient has been given 2 quarts (about 2 liters) of orange and grapefruit juice daily for the past four days

DISCUSSION

DR WALTER F LEVER, Boston I suggest the diagnosis of Majocchi's disease In scurvy one has massive bleeding into the skin Here they are hemorrhagic punctate dots and erythema, as are commonly seen in Majocchi's disease

DR JOSEPH GOODMAN, Boston I agree that the lesions resembled Majocchi's disease, but in my opinion the patient has symptomatic purpura Whether or not he had scurvy could have been ascertained by a vitamin C determination, which was not on the record Since the treatment it would be impossible to say whether he had scurvy Follicular hemorrhages are characteristics of that disease

DR GEORGE E MORRIS, Boston When this man was seen last week he had the follicular hemorrhages which are typical of scurvy One may find large ecchymoses, but it is typically a punctate hemorrhagic disease Last week the result of a tourniquet test was strongly positive The patient was given a diet rich in vitamin C against my orders, and the result of the tourniquet test is now negative The eruption is disappearing That is not typical of Majocchi's disease

Dermatophytosis of the Extremities, Due to Trichophyton Purpureum

Presented by DR SEYMOUR J WHITE, Lawrence, Mass

An intradermal injection of 0 1 cc of Lederle's diagnostic trichophytin extract (1 30) gave rise to an immediate wheal reaction, within ten minutes it measured 1 5 cm in diameter, and numerous pseudopods soon appeared This reaction remained about twelve hours and left a persistent, erythematous, scaly patch, the result of a control injection of isotonic sodium chloride solution was negative Scales removed from the right palm and planted on Sabouraud's medium produced a growth identified as Trichophyton purpureum A biopsy specimen obtained from the left knee exhibited only nonspecific inflammation A number of fungicidal remedies have been applied for prolonged periods of time without response

DISCUSSION

DR JACOB H SWARTZ, Boston I suggest that the mycologic diagnosis be held in abeyance until the culture is more characteristic These lesions do simulate those seen with infection by the organism of Trichophyton rubrum (or T purpureum), but it might be Trichophyton gypseum

DR WALTER F LEVER, Boston Dr Swartz, do I understand that T rubrum or purpureum does not cause sensitization?

DR JACOB H SWARTZ, Boston That is correct, and I would not pay much attention to the immediate reaction A diagnosis should not be made on the cutaneous test alone, and I cannot do so on the strength of the culture as yet

DR FRANCIS P MCCARTHY, Boston Is this organism a possible contaminant or a true pathogen? I should like to know whether it is found on the skin normally

DR JACOB H SWARTZ, Boston I have never seen it as a contaminant

DR JOHN G DOWNING, Boston My co-workers and I cultured 100 specimens of normal skin of patients who had never had a fungous infection Specimens were taken from the scalp, the corners of the mouth, between the toes and the soles Pathogenic fungi were found in 2 cases, neither T purpureum nor Monila albicans (Candida) was isolated

until October 1947, when a lesion appeared on the left heel which was subsequently diagnosed in the Boston City Hospital as yaws Another lesion was discovered on the left buccal mucous membrane at that time

When examined in October, this little boy revealed a superficial ulcer on the left heel It was 1 5 by 1 5 cm , with slightly elevated margins and was not tender Treatment was not started for about a week, and during that time the entire lesion became raised, with the appearance of a chronic granuloma, and was distinctly indurated The lesion on the left buccal mucous membrane consisted of a shallow ulceration measuring 6 by 6 mm , no induration could be detected There were numerous enlarged, nontender posterior cervical and inguinal lymph nodes At present there is nothing on the left heel except a trace of deeper pigmentation The buccal mucous membrane exhibits no change of any kind

Dark field examination revealed organisms indistinguishable from Treponema pallidum The Hinton and Kahn reactions of the blood were repeatedly positive The white cell count of the blood was 13,400, and the red cells numbered 3,640,000 per cubic mm , a differential smear contained 48 per cent polymorphonuclear leukocytes, 50 per cent lymphocytes and 2 per cent monocytes Treatment consisted in administration of 4,000,000 units of penicillin by intramuscular injection

DISCUSSION OF CASES OF FRAMBESIA TROPICA

DR JOHN G DOWNING, Boston At the June Meeting of the American Dermatological Association, Dr Rein reported a series of 1,000 cases of yaws, in all of which the clinical lesions disappeared under treatment, but the serologic reactions became negative in only 15 per cent He gave 1,200,000 Oxford units In the discussion of that report, others who had had experience with yaws stated that the reactions of as high as 40 per cent of their patients remained positive It was clearly indicated that large doses of penicillin are needed to cure this disease, greater quantities will result in better clinical and serologic response

Tuberculosis Luposa Presented by DR. JOSEPH GOODMAN, Boston

Idiopathic Macular Atrophy of Skin Presented by DR WILLIAM R HILL, Boston

Hemangiolymphangioma of Skin Presented by DR S J MESSINA, Boston

A Case for Diagnosis (Mycosis Fungoides or Late Cutaneous Syphilis?) Presented by DR WILLIAM R HILL, Boston

Lupus Erythematosus, Restricted to Lips Presented by DR G MARSHALL CRAWFORD, Brookline, Mass

W G , a 23 year old white American student, presents lesions on his lips of six years' duration This difficulty began as a single fissure in the center of the upper lip which refused to heal It became worse every summer and was aggravated by any exposure to heat At first it would heal in the winter, but it has become worse with the passage of time and now does not heal at any time The fissure spread to become a raw area which slowly extended inward and upward It has been most uncomfortable throughout most of this time, and the greatest discomfort is on the inner aspect of the upper lip Smaller lateral lesions appeared later Two years ago the area measured 2 cm in length (transversely) and was

Leukoplakia of the Penis. Presented by DR JOHN G DOWNING, Boston

J F, a 65 year old white man of Irish birth, a retired elevated railway conductor, is presented with the complaint of soreness and cracking of the prepuce for about two months The patient had applied only petrolatum This afforded no relief, and the condition had become steadily worse

Examination reveals a distinct thinning of the skin of the prepuce and also of the glans penis There is a constricting sclerotic band about 2 cm proximal to the free edge of the prepuce, this has been partially relieved by biopsy, and at that point where the biopsy specimen was taken there is a small crust The remainder of this band is characterized by the appearance of whitish plaques and streaks with several erosions and fissures

The diagnosis from histologic study was reported as leukoplakia There has been no treatment

DISCUSSION

DR FRANCIS P MCCARTHY, Boston Leukoplakia resembles kraurosis in the aged in the sense that there are interstitial changes and leukoplakia and erosion

DR BERNARD APPEL, Lynn The diagnosis of kraurosis of the prepuce was considered The microscopic examination ruled that out, because it did not show typical changes of kraurosis or atrophy

DR FRANCIS P MCCARTHY, Boston The depth of the biopsy specimen may be misleading A deep section is essential and special connective tissue stains are required in order to rule out kraurosis In spite of the histologic changes, I feel that this is kraurosis of the prepuce

DR WALTER F LEVER, Boston I would oppose the diagnosis of kraurosis The histologic picture of kraurosis is characterized by atrophy of the epidermis and degeneration of the collagen In this case there was neither The epidermis was acanthotic, and there was considerable hyperkeratosis The biopsy specimen extended a fair depth into the connective tissue, and it showed no evidence of degeneration There were numerous dilated capillaries and a chronic inflammatory infiltrate There was no evidence of carcinoma The histologic picture is consistent with senile keratosis or leukoplakia

DR FRANCIS P MCCARTHY, Boston In kraurosis there may be areas of atrophy and also leukoplakia with both hyperkeratosis and acanthosis

DR JACOB H SWARTZ, Boston I agree

DR JOHN G DOWNING, Boston There was no evidence of kraurosis or atrophy The skin was infiltrated, fissured and leukoplakic in appearance It probably would go on to cancerous degeneration if neglected This patient can be cured by excising the area affected

Leukoplakia of the Tongue, Buccal Mucosa and Lips, Syphilis Presented by DR F RONCHESE, Providence, R I

A D, a 38 year old white man of American birth, a truck driver, for the past three years had noted white patches on his tongue and lips and on the inside of his mouth The anterior portion of the tongue was raw for much of this time and was somewhat tender, but there was otherwise little discomfort Shortly after the appearance of these lesions the patient was found to have repeatedly positive serologic reactions to tests for syphilis No history referable to the date of infection was obtainable, previous genital or cutaneous lesions were denied No other relevant data were obtained The patient smoked from eight to ten cigars daily

about 5 mm in width The patient was subsequently on naval duty in the tropics, and his lip became so badly swollen that he was incapacitated much of the time He was finally sent back to the United States for that reason The lower lip became involved while he was in the South Pacific, but the condition has never been as severe as on the upper lip

At the present time the external appearance of the lips is grossly normal except for slight edema of the upper lip The inner aspect of the latter reveals intense erythema involving the two center fourths of the lip There is a depression within the affected area as though it had been drawn inward by scarring, but no scarring can be definitely made out A mild degree of maceration is present, and the affected area appears abraded The lower lip is similarly but much more mildly affected and only along the occlusal surface

This is a private patient who was seen in consultation, and there was no opportunity permitted for laboratory study None has been carried out elsewhere Treatment in the past has consisted of liver injections, arsenic drops, several unknown injections, great quantities of vitamins and roentgen ray therapy More recently injections of a gold preparation have been given (quantity unknown), these were stopped because of local reactions at the affected site In the last few months, the patient has received oxophenarsine hydrochloride (mapharsen®), and he feels that this has been responsible for slight improvement

DISCUSSION

Dr Bernard Appel, Lynn, Mass I have only an unhappy prediction to make In my experience in several similar cases the prognosis is bad The disease persists, and nothing I know of has done any of the patients any good

Dr John G Downing, Boston On close examination, the glandular orifices are plainly visible, owing to dilatation of the ducts There is a sticky secretion My diagnosis is cheilitis glandularis apostematosa

Dr William R Hill, Boston In the last two years I have observed 4 patients with dermatitis of the lips somewhat similar to that which this patient presents Three patients related the onset of their eruption to exposure to sun Two were sailors in the Caribbean area, and their disease was diagnosed as lupus erythematosus, they were treated with bismuth and gold preparations without response During the period of observation 1 of these men had a typical eruption of allergic eczema on the back of the hands, and the thought occurred to me that perhaps the disease was a virus infection With this in mind, I treated 2 patients with smallpox vaccine but noted no improvement

Dr G Marshall Crawford, Brookline, Mass This man is not my patient I saw him five or six years ago when his complaint first began and there was nothing present except a small fissure which had healed during the winter months and then recurred He went to war but was discharged from the service because of these lips, receiving treatment from several sources as indicated in the history I recently saw him again in consultation I was not satisfied with the diagnosis as presented, and yet I could not deny it Nevertheless, I think that there is a possibility that he may not have lupus erythematosus Without other lesions, the disease is an enigma

Dr William R Hill, Boston Does the fact that the lips respond to bismuth or gold help in the diagnosis of lupus erythematosus?

Dr Maurice M Tolman, Boston I have searched steadily for a case of lupus erythematosus discoides limited to the mucous membrane I have heard of such cases but have yet to see one I am inclined to think this is not lupus ery the-

The distal half of the dorsal aspect of this man's tongue is almost completely denuded of epithelium Within this area there are numerous small, white, infiltrated islands and some atrophic scarring The entire distal half of the tongue appears somewhat shrunken and atrophic, the margins are slightly elevated and are marked with alternate red and pearly gray striations The patient's lips and buccal mucosa also exhibit scattered small plaques of white atrophic tissue

Treatment has been carried on by the patient's family physician It consisted of fifty-five injections of bismuth salicylate and thirteen of oxophenarsine hydrochloride (mapharsen®) between May 1943 and October 1945 The dosage of these treatments was not known, there had been no clinical improvement The patient was smoking less during that time In March 1947 3,000,000 units of penicillin in oil and wax were administered, without detectable effect on the oral changes

The Hinton and Kahn reactions of the blood had both remained consistently positive up to the time of presentation Histologic examination of a biopsy specimen taken from the tongue revealed the following changes consistent with leukoplakia, acute ulceration and inflammation of the mucosa, with no evidence of malignancy

DISCUSSION

DR FRANCIS P MCCARTHY, Boston The erosion on this patient's tongue came on suddenly, and the ulceration has continued for three years As a result of inadequate treatment for syphilis there developed a smooth atrophy suggestive of glossitis luetica atrophica The failure of the ulceration to heal may be explained by interstitial connective tissue changes associated with limited blood supply from an old endarteritis I have recently studied syphilitic glossitis in postmortem specimens wherein interstitial sclerosis associated with decided narrowing of the lumen of arteries and atrophy of the overlying papillae are constantly found The granulation tissue as seen in this case does not become malignant, but the leukoplakic lesions in the periphery of the lesion may show a malignant tendency

DR JOHN G DOWNING, Boston When I first saw this man's tongue I was impressed by the sharp outline of the granulations and the intervening islands of leukoplakia I ordered two biopsies to eliminate malignancy, the diagnosis from both specimens was chronic inflammation I might suggest a diagnosis of stomatitis factitia I have seen 3 cases in which this condition was proved to be self-inflicted This man has syphilis, and I believe that he has been applying some strong chemical to his tongue to remove the previous leukoplakia

DR FRANCIS M THURMON, Boston Around the denuded areas there is definite leukoplakia of the tongue I think that the prognosis is serious, because once cancer of the tongue develops in a patient with tertiary syphilis there is no treatment that is successful

DR FRANCIS P MCCARTHY, Boston I am interested in what Dr Downing said because it seems unusual to see granulation continue so long without healing The blood supply is greatly diminished, and that may be a factor Why anyone should inflict a lesion of this kind on his own tongue is difficult to understand without some compelling motive such as the collection of compensation The patient told me that it developed overnight

DR F RONCHESE, Providence, R I If the changes on this man's tongue are regarded as potentially malignant, the entire surface should be removed with the coagulating loupe

DR JOHN G DOWNING, Boston Syphilis is in the background of this disease of the tongue, aggravated by a therapeutic attempt to cure it

matosus This man has a protruding lower lip I have seen a number of men within the ages of 18 to 25 with carcinomatous degeneration of the lower lip following extensive exposure to sun I have also seen lupus erythematosus of the lip which soon developed into carcinoma, and I think this patient will have carcinoma Lupus erythematosus of the mucous membrane does not respond well to bismuth

DR BERNARD APPEL, Lynn, Mass Several years ago I saw a middle-aged woman with lesions on the inner aspect of the lower lip that looked like either lichen planus or the climacteric type of leukoplakia The eruption turned into a more classic lichen planus and subsequently spread onto the buccal mucosa A biopsy was done and the microscopic examination showed either lupus erytnematosus or chronic inflammatory reaction of mucous membrane It was not until two or three years later that the lesions finally extended onto and beyond the vermilion borders of both lips, showing the classic cutaneous changes Although, strictly speaking, that disease was not limited to the mucous membrane, nevertheless it started there and was localized there for a long time Going back to the present case, I feel that this is more likely to be lupus erythematosus of the mucosa and less likely to be carcinoma of the lip

Pityriasis Rubra Pilaris Presented by DR LEON BABALIAN, Portland, Maine

Lichen Nitidus Presented by DR E A LAFRENIERE, Arlington, Mass

Lichen Planus Presented by DR GEORGE MORRIS, Boston

Case for Diagnosis (Nevus Linearis? Linear Lichen Planus?) Presented by DR GEORGE MORRIS, Boston

Multiple Idiopathic Hemorrhagic Sarcoma of Skin Presented by DR G MARSHALL CRAWFORD, Brookline, Mass

Pseudoxanthoma Elasticum of the Neck with Angioid Streaks Presented by DR JOHN ADAMS JR, Boston

This case provides a classic picture of pseudoxanthoma elasticum, first described by Balzer in 1884 It may be located on the flexor folds, the axillas, the upper and inner surfaces of the thighs and the abdomen, and in very rare cases the mucous membranes are also affected The lesions are asymptomatic but may persist for years Areas of calcification have been reported in the affected parts The angioid streaks of the retina, as noted in this patient, occur in about 25 per cent of the cases They are probably a part of a generally defective elastic tissue Hypertension may be found in some of the patients and also degeneration of the elastica of the larger arteries This might account for the hemorrhages which occur in various organs, including the brain The cause is unknown, and the disease is harmless

Leukemia Cutis (Type Unspecified) Presented (by invitation) by DR PAUL J CATINELLA, Boston

Lymphatic Leukemia with Herpes Zoster, Generalized Presented by DR S J MESSINA, Boston

DR FRANCIS P MCCARTHY, Boston That is a reasonable explanation, and the factitial element in this case may explain the unusual findings

Psoriasis, Keloids Following "Injections" Presented by DR LEO KORETSKY, Chelsea, Mass

A Case for Diagnosis (Erythema Multiforme Exudativum? Bullous Impetigo?) Presented by DR GEORGE SCHWARTZ, Malden, Mass

DISCUSSION

DR MILDRED L RYAN, Brockton, Mass I think that this 3 year old child has dermatitis medicamentosa She has had frequent attacks of asthma Has she been given any iodides or bromides?

DR GEORGE SCHWARTZ, Malden, Mass I saw this girl ten days ago At that time she presented bullae of ½ to ¾ inches (1 to 2 cm) in diameter, arising from normal skin They were on the arms, legs, abdomen and neck, there also were six or eight vesicles on the scalp I found nits and thought that she had bullous impetigo I have not seen her since then, and today she shows a different picture, one would think that she was another patient

DR S J MESSINA, Boston I think that this is a case of Loeffler's syndrome She had a high eosinophilic count and a history of asthma, which are characteristic of that disease There may or may not be an eruption which can suggest erythema multiforme I think that Loeffler's syndrome is a strong possibility in this case

DR JOHN G DOWNING, Boston I agree with the diagnosis of Loeffler's syndrome Recently I saw a patient with a history of asthmatic attacks, mottling on the chest and an eruption resembling erythema perstans on the chest, the blood picture showed a high eosinophil count

Dr Francis M Thurmon, *President*

Dr G Marshall Crawford, *Secretary*

New Haven, Conn, Oct 8, 1947

A Case for Diagnosis (Xanthomatosis?) Presented by DR MAURICE J STRAUSS, New Haven, Conn

E C, a 2 year old white girl, acquired a solitary lesion on the right cheek at about the age of 4 months This slowly increased in size, and gradually a few similar lesions developed around the original one The latter attained a size of 9 by 6 mm before excision six months ago They have been asymptomatic

On the right cheek there is a group of six small, solid, slightly elevated brownish red nodules each about 4 or 5 mm in diameter

Histologic examination revealed only a chronic inflammatory reaction

DISCUSSION

DR LEON BABALIAN, Portland, Me Although there is no regional enlargement of lymph nodes in this case, it is difficult to rule out lupus vulgaris

DR ALFRED HOLLANDER, Springfield, Mass My opinion is that these lesions belong to the group of localized xanthoma I did not study the slide too well, but the section did show some foam cells

Chronic Pyoderma (Staphylococcus Aureus) Presented by DR GEORGE MORRIS, Boston

A Case for Diagnosis (Sarcoid? Tuberculid?) Presented by DR BERNARD APPEL, Lynn, Mass

Hodgkin's Disease of the Skin Presented (by invitation) by DR PAUL J CATINELLA, Boston

D F, a 34 year old white housewife of Irish birth, presents a lesion on the front of the left thigh which is said to be of only nine weeks' duration It appeared first to be a small blister and then became a shallow ulcer which gradually enlarged The lesion had been asymptomatic

At the time of first examination, several weeks ago, a solitary lesion was found on the anteromedial aspect of the patient's left thigh about 4 inches distal to the inguinal ligament This proved to be a moderately shallow circular ulcer of 2 5 cm diameter The center portion of the base of the ulcer was slightly raised, granulomatous and moist on the surface The borders were firm, and the tissue about the periphery was deeply infiltrated

A biopsy specimen was obtained, and the histopathologic examination revealed changes indicating a diagnosis of Hodgkin's sarcoma The white cell count of the blood was 2,750 per cubic millimeter, a differential smear revealed 56 per cent polymorphonuclear leukocytes, 38 per cent lymphocytes, 3 per cent monocytes and 3 per cent eosinophils Roentgenologic examination of the chest, lumbosacral portion of the spine, pelvis and hips revealed nothing abnormal except a "condensing osteitis of the right ilium"

The patient's lesion was widely excised two weeks ago The scar is soft, without suggestion of recurrence

DISCUSSION

DR FRANCIS M THURMON, Boston What is the prognosis in this case?

DR JOHN G DOWNING, Boston We should raise the question of further therapy at this point Have sufficient measures been taken?

DR BERNARD APPEL, Lynn, Mass When I first saw the patient, I considered this to be syphilis, probably an unusual extragenital chancre A week or so later this was an oozing, exuberant, red, moist, granulating, mushroom type of lesion with the edges firm and curled outward, and then it looked like either a rapidly growing carcinoma or sporotrichosis, or perhaps one of the other mycotic granulomas The last thing in my mind was Hodgkin's disease, and when I heard the microscopic diagnosis I could hardly believe it, yet the slide shows cells of the immature lymphoblastoma type that are consistent with Hodgkin's disease

DR MAURICE J STRAUSS, New Haven, Conn As the patient was presented today, there was no lesion to be seen However, having now looked at the colored photograph, I feel that we would be justified in making a diagnosis of mycosis fungoides of the tumor d'emblee type It is not always easy to tell mycosis fungoides from Hodgkin's disease microscopically, and it is quite possible that this error could occur I recall a similar case presented to this Society several years ago at a meeting at New Haven, Conn The man died six years later, I believe in an accident, and had never had any known recurrences The lesion was in the lumbar region, and a simple but wide excision was performed with skin grafting

DR E MYLES STANDISH, Hartford, Conn I recall that about fifteen years ago I saw an almost exact counterpart of this lesion as far as color and induration are concerned, it proved to be lupus vulgaris

DR JOSEPH MULLER, Worcester, Mass I also thought of tuberculosis, but with pressure under a glass slide there was absolutely no sign of the typical apple jelly color that lupus vulgaris should show

DR ELLWOOD C WEISE, Bridgeport, Conn Although the light was poor where this little girl was shown, I thought that I could see a number of comedos in the affected area I have seen cases of precocious acne accompanied with chronic granulomatous lesions which were similar in appearance

DR BERNARD APPEL, Lynn, Mass I had the same first impression, but then I moved the baby into better light and saw that these pinpoint black dots were not comedos but little deposits of pigment My next feeling was that this was a nevus xanthomatosus I did not see the slide, but I do not consider the presence of foam cells essential

DR G MARSHALL CRAWFORD, Brookline, Mass There were definite small pigmentary deposits The possibility of a sebaceous nevus came to mind in view of the yellowish red color and firm consistency of the nodules I searched the section for foam cells but saw only a number of large pale reticulated structures which suggested portions of sebaceous glands cut at the edges

DR JACOB H SWARTZ, Boston This lesion may be given several different names It does not matter whether it is called nevus comedonicus or a sebaceous nevus, it falls into the same group I do not believe that a foam cell will ever be found

Granuloma Annulare Presented by DR MAURICE J STRAUSS, New Haven, Conn

Keratosis Follicularis Presented by DR ALBERT LEVENSON, Bridgeport, Conn

Dermatitis Herpetiformis Presented by DR CHARLES N SULLIVAN, New Britain, Conn

E S, a 42 year old white printer, first had severely pruritic lesions on the back of the left thigh four years ago, the eruption slowly spread and became generalized There have been several remissions and exacerbations, but the eruption has never completely cleared

There are groups of crusted papules, each lesion about 2 to 3 mm in diameter, scattered profusely over the trunk and extremities On the cheeks there are vesicles, some recently abraded and crusted There are many macular scars with pigmentation

Examination of the blood revealed nothing abnormal except 11 per cent eosinophils Microscopic examination of a biopsy specimen, reported by Dr Wilbert Sachs, of New York, showed the vessels of the middle and upper parts of the cutis dilated and the walls slightly thickened There was a perivascular infiltrate of small round cells and wandering connective tissue cells There was moderate interstitial edema in the upper part of the cutis The epidermis was regularly acanthotic, with an impetiginized cavity which had partially broken through at one point

Sulfapyridine relieved the pruritus but produced urticaria Sulfadiazine and roentgen ray treatment produced a remission, but the eruption recurred when this

For all practical purposes, that is what has been done upon the patient presented today, and it may well be all the treatment that will be necessary

DR WALTER F LEVER, Boston The histologic section was densely infiltrated with anaplastic and immature reticulum cells Some of them had large nuclei, and others were multinucleated It is perhaps best to call this lesion a reticulum cell lymphoma Concerning the prognosis, I agree with Dr Strauss It is not uncommon for reticulum cell lymphoma to start as a single lesion on the skin or elsewhere, and if this lesion is excised completely there may be no recurrence

DR LEON BABALIAN, Portland, Maine Dr MacKee advised wide excision followed by irradiation

DR WALTER F LEVER, Boston I do not believe that irradiation is generally done Most lesions are in lymph nodes, where irradiation is impractical Radical excision is best, irradiation is optional

DR BERNARD APPEL, Lynn, Mass The matter of terminology of this group of tumors is still undecided When the proponents of the various terms get together and agree on what to call these cells, they may find that they are all talking about the same thing I think that if Dr Catinella were to go to the pathology department of the hospital with which I am associated and look up the original biopsy slides, he would find that they correspond closely to the section exhibited today Many of us have seen a solitary lymphoblastoma cured by surgical excision This will probably turn out to be that type of case

DR PAUL J CATINELLA, Boston (by invitation) I am sorry that the members did not have the benefit of all of the slides Sections of specimens taken a week later showed a picture resembling reticulum cell sarcoma except for one feature which established the diagnosis of Hodgkin's sarcoma That was the presence of multinucleated and polymorphonuclear giant cells of the Dorothy Reed type Wide excision was advised in the hope that if the lesion had started in the skin, eradication of the primary focus might be followed by a cure It was a long chance If the condition were not treated, the prognosis for life would vary from one to three years

DR JOHN G DOWNING, Boston The most complete monograph on lymphomas is that of Jackson and Parker (Jackson, H, Jr, and Parker, F, Jr Hodgkin's Disease and Allied Disorders, New York, Oxford University Press, 1947) It covers about every phase of this group of diseases, is clearcut and presents a clever classification according to life expectancy The reason I inquired about treatment is that we consulted Jackson, and he suggested excision, adding that the quicker excised, the more chance this patient had of living

Keratosis Follicularis Presented by DR FRANCIS M THURMON, Boston

Aneurysm of Transverse Aorta Presented by DR GEORGE MORRIS, Boston

Xanthoma Diabeticorum and Lipemic Retinitis Due to Diabetes Mellitus Presented by DR BERNARD APPEL, Lynn, Mass

Psoriasis in a West Indian Negro Presented by DR S J MESSINA, Boston

Sarcoidosis of the Skin Presented by DR WALTER F LEVER, Boston

treatment was discontinued Tripelennamine hydrochloride (pyribenzamine hydrochloride®), 50 mg four times a day, is of slight value at this time

DISCUSSION

DR BERNARD APPEL, Lynn, Mass I think that the case is clinically typical of dermatitis herpetiformis and accept the diagnosis as presented The patient said urticarial reactions were so severe that he was completely covered with wheals Since sulfapyridine produces such a reaction, I suggest that tripelennamine hydrochloride be used in appropriate doses, I should prescribe 600 or 800 mg daily A patient with dermatitis herpetiformis who took sulfapyridine with fairly good results was recently given diphenhydramine hydrochloride (benadryl hydrochloride®) for a comparison She noted more lasting relief and recession of the lesions than with sulfapyridine One expects some trouble from sulfonamide drugs, and it is much safer to use tripelennamine or diphenhydramine in large doses

DR MAURICE M TOLMAN, Boston Since 1938 I have had under personal observation 3 patients with dermatitis herpetiformis who have taken sulfapyridine continually without reaction, and it controlled their disease I am a little afraid of continuing its use indefinitely We decided to try diphenhydramine and tripelennamine in doses of 600 mg daily in carefully controlled patients in the hospital but observed no relief from pruritus or diminution of the lesions We then administered sulfapyridine, there was immediate response, and remission took place

DR JOSEPH GOODMAN, Boston On the other side of the picture, I should like to mention a patient who took sufficient sulfapyridine to produce a blood level of 7 mg per hundred cubic centimeters with but little effect on the dermatitis herpetiformis That patient has responded better to 400 mg of diphenhydramine daily than to the large doses of sulfapyridine One must thus conclude that some patients do better with one drug and some with the other I cannot maintain that sulfapyridine controls the disease in all patients with dermatitis herpetiformis, the same is true of tripelennamine and diphenhydramine

DR NEVILLE KIRSCH, Hartford, Conn Some physicians in general practice have treated dermatitis herpetiformis with nicotinic acid

Hemangiolymphangioma of Tongue Presented by DR MAURICE J STRAUSS, New Haven, Conn

Sarcoidosis of Skin Presented by DR E MYLES STANDISH, Hartford, Conn

Adenoma Sebaceum Presented by DR MAURICE J STRAUSS and (by invitation) DR LOUIS O'BRASKY, New Haven, Conn

H M is a 12 year old white school girl About two months after she was born, her parents first noticed thickening under the toe nails and finger nails At the age of 7 years, papules appeared on the face Both parents are living and well and have no lesions of the skin although both are mentally defective One brother has a speech defect and is classified as mentally defective but shows no cutaneous abnormality Two brothers and two sisters are mentally and physically normal The patient herself is mentally normal

On the face there are numerous groups of small discrete white papules, symmetrically distributed over the forehead, on the sides of the nose and on the zygoma All the nails of the hands and feet are thin, soft and discolored, especially the nails of the great toes, and their growth is retarded There are brown fibrotic

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

Herman Sharlit, M D , *Chairman*

Maurice J Costello, M D , *Secretary*

Jan 7, 1947

Erythema Induratum Without Ulceration Presented by Dr Maurice J Costello

P M , a Puerto Rican woman aged 27, is presented from the Dermatologic Clinic of Bellevue Hospital with an eruption involving the thighs and the lower third of each leg of about one year's duration The patient had pulmonary tuberculosis ten years ago, but she states that a recent roentgenogram of her chest showed arrested pulmonary disease, and examinations of the sputum did not reveal tubercle bacilli Her menses are normal A brother and sister died of tuberculosis

The patient states that her eruption began as small red papules which were painful and frequently broke down and drained pus (This was not verified in the four months the patient has been under observation in this clinic) The lesions become painful when she arises each morning and also on exposure to cold

The eruption is present on the lower thirds of the legs and about the ankles and consists of scattered, erythematous, scaly, nodular and plaque-like lesions, some of which are fluctuant but do not drain pus Others are indurated

A section of the skin showed mild acanthosis of the epithelium, with some downgrowth of the rete pegs into the corium In the superficial and deep corium numerous granulomatous lesions were seen These consisted of indistinct epithelioid cells with occasional multinucleated giant cells in the central portions There was some proliferation of fibrous tissues and young blood vessels about these nodules A moderate infiltration of lymphocytes and large mononuclear cells and a few polymorphonuclear and plasma cells were present throughout the corium but primarily in the granulomatous lesions In and about the lesions there were varying numbers of mononuclear cells filled with brown granular pigment Deep in the corium some normal adipose and glandular tissue was seen Elastic tissue staining revealed the absence of elastic fibers through the upper corium wherein the tubercles were seen The histologic diagnosis was erythema induratum

The patient underwent thoracoplasty about ten years previously A roentgenogram of the chest three days ago showed no activity

DISCUSSION

Dr S Irgang It is not possible to make a definite diagnosis of erythema induratum in this case because the subcutis was not included in the section That is the layer in which the typical changes of this disease are found

Dr Fred Wise The diagnosis of erythema induratum is made in this case by clinical observation alone I should say that this is the typical textbook picture of erythema induratum of the Bazin type The characteristic histologic changes occur in the deeper veins especially, but a clinical diagnosis is acceptable in this instance A histologic diagnosis can be made, even in the absence of tubercle formation

tumors under most of the nails, elevating the plate from the bed The extensor surfaces of the arms and legs, the back and the buttocks are dry with follicular hyperkeratosis

Examinations of the blood and urine showed normal conditions The Kahn reaction of the blood was negative

DISCUSSION

DR ALBERT LEVENSON, Bridgeport, Conn I should call this a case of milium Clinically the lesions do not resemble those of Pringle's adenoma sebaceum

DR ALFRED HOLLANDER, Springfield, Mass I definitely exclude Pringle's disease I feel especially that the numerous lesions on the forehead are those so often seen in the common type of acne and that if one tried to remove them, one would find some to be comedos, some to be milium-like and some to be hygromas Further inspection of the face revealed other small comedo-like lesions The lesions on the face fall partly into the acne group and partly into the hygroma group Those on the forearms should be classified as keratosis pilaris

DR G MARSHALL CRAWFORD, Brookline, Mass I agree with what has been said, but I insist on the diagnosis of tuberous sclerosis, also making a plea that all such cases be called tuberous sclerosis Adenoma sebaceum and other subsidiary diagnoses may be added as presented by each individual patient The cutaneous and visceral anomalies reported in cases of tuberous sclerosis are almost beyond enumeration A wide variety of cutaneous changes occur Most characteristic are the subungual keratoses which in this girl involve every one of her twenty nail beds She does not show the characteristic adenoma sebaceum, as every one else has said The milium-like changes do not exclude the diagnosis of tuberous sclerosis, neither do the keratosis-pilaris-like changes, which in this case are not limited to the usual areas but are diffuse The entire skin shows varying degrees of follicular hyperkeratosis There is also a background of mental deficiency and other abnormalities, which is entirely characteristic of tuberous sclerosis

DR EARL GLICKLICH, Boston I have observed a case of adenoma sebaceum in which it was necessary to have fundus examinations for additional information to make a diagnosis Such an examination usually shows a strawberry or mulberry type of growth on the fundi I suggest that an ophthalmologist examine this patient's eyegrounds

DR G MARSHALL CRAWFORD, Brookline, Mass There should also be roentgen examinations of the chest and kidneys, since polycystic kidneys and various other visceral changes are much commoner than is usually supposed

Erythroplasia of Queyrat, Penile Presented by DR MAURICE J STRAUSS, New Haven, Conn

Dermatitis Exfoliativa Presented by DR MICHAEL J MORRISSEY and DR HARRY S REYNOLDS, Hartford, Conn

Squamous Cell Carcinoma of Leg, Blastomycosis? Presented by DR ELLWOOD C WEISE, Bridgeport, Conn

Multiple Idiopathic Hemorrhagic Sarcoma of Skin Presented by DR MAURICE J STRAUSS, New Haven, Conn

DR S IRGANG In the absence of ulceration, it is not possible to differentiate erythema induratum clinically from nodular nonsuppurative panniculitis In view of the equal distribution of lesions about the legs and also because of the absence of a single ulcerated lesion during a period of fourteen months, I favor a clinical diagnosis of nodular nonsuppurative panniculitis

DR CHARLES WOLF To make a diagnosis of erythema induratum without real corroboration is rather risky I had the experience recently with a patient who had a solitary lesion on the calf of the leg for six months, with a history of pulmonary tuberculosis and thoracoplasty I took it for granted that the lesion was erythema induratum I was to perform a biopsy, but after one visit the lesion healed so much that I thought biopsy unnecessary The surgeon thought the patient should go back into the hospital for further operative treatment because of infection in the pleura I told him the cutaneous lesion was a manifestation of tuberculosis, and he removed it while operating on the chest Biopsy revealed chronic inflammatory tissue The patient presented tonight may have undergone a thoracoplasty, but the lesion on the leg may be an entirely different entity Therefore, we must have further evidence before we can accept it as Bazin's disease

DR FRANK C COMBES There is a remote possibility that this is not erythema induratum, but from a clinical standpoint I cannot favor any other diagnosis I will admit that this disease has its inception in the subcutis, but, as I understand it, the histologic section conformed to the changes seen in erythema induratum Because of its typical clinical features, I would agree with the diagnosis as presented, even if the histologic picture did not support it

DR TIMOTHY J RIORDAN I believe that is an adequate description, and the condition can be interpreted as Bazin's disease After all, the pathologic changes can be tuberculoid or tuberculous One does depend on the deep site of the biopsy material, and all that is necessary is to find changes in the region of the deep cutis, the region of the deep plexus of blood vessels It is true that it is best to include adipose tissue However, if by chance enough of the deep corium is got to correspond with the description given tonight, I would certainly accept it as erythema induratum, or Bazin's disease In my experience with erythema induratum tubercle formation or an entirely tuberculoid type of reaction may be present Often the diagnosis can be made without the appearance of classic tubercles as we know them, with caseation necrosis or pure epithelioid structure Inflammatory changes plus involvement of the blood vessels, tuberculoid reaction plus blood vessel reaction, or tuberculous reaction plus blood vessel reaction can establish the diagnosis

DR ISADORE ROSEN I agree with those who believe, on clinical grounds, that this patient is suffering from Bazin's disease When lesions of this disease break down, they frequently resemble gummas, and even on microscopic examination it is difficult to distinguish them from lesions of syphilis

DR MAURICE J COSTELLO I do not know how far Dr Irgang expected us to go in taking a biopsy, but, as Dr Rosen just indicated, I have seen lesions of papulonecrotic tuberculid accompanied with lesions of typical erythema induratum in the same patient

A Case for Diagnosis (Erythema Induratum? Pressure Grooves on the Sides of the Legs) Presented by DR MAURICE J COSTELLO

Multiple Idiopathic Hemorrhagic Sarcoma of Skin Presented by DR M J MORRISSEY and DR H S REYNOLDS, Hartford, Conn

Aphthous Stomatitis Presented by DR MAURICE J STRAUSS, New Haven, Conn

Alopecia Cicatrisata Presented by DR MAURICE J STRAUSS, New Haven, Conn

Acarophobia Presented by DR ELLWOOD C WEISE, Bridgeport, Conn

Blastomycosis of the Skin Presented by DR MAURICE J STRAUSS and (by invitation) DR HARRY SIGEL, New Haven, Conn

H M, a 23 year old white electrician, first noticed a "pimple" on his left shoulder about a year ago For six months immediately preceding the development of this lesion he lived in Connecticut From September 1945 to February 1946 he was in Korea and from March to September 1945 in Okinawa Prior to that he lived in Idaho While in Okinawa, some "sores" developed on the back of his neck and on the extensor surfaces of both hands These healed spontaneously within about six weeks The lesion which marked the onset of the present condition grew slowly and progressively As the border extended, the central portion partly healed

There is now a large lesion on the left shoulder, about 18 cm long and 10 cm wide The border is circinate, bluish red, raised, rolled and indurated The marginal elevation slopes gradually toward the center of the lesion The border is most prominent at its medial edge, and there it appears somewhat verrucous Several portions of the margin are tender and exude small drops of pus on pressure The lateral edge of this lesion is flatter and more cicatricial

Direct microscopic examination of exudate from the lesion showed round, thick-walled, budding cells Cultural studies yielded a typical growth of Blastomyces dermatitidis hyphal with chlamydospores at room temperature and budding cells when incubated There has been no treatment administered

DISCUSSION

DR JACOB H SWARTZ, Boston I saw the slides and culture mounts and agree with the diagnosis of blastomycosis The culture was difficult to identify, as are all cultures in such cases The one grown at room temperature showed the hyphal type of growth with chlamydospores The one grown on Sabouraud's medium at incubator temperature exhibited the typical budding cells which are characteristic of Blastomyces Clinically the lesion was also compatible, with wartlike projections from the border The question at present is how to cure it I suggest a combination of sulfonamide drugs and roentgen rays Beyond that, I suggest ethyl iodide by inhalation Excision would be satisfactory if the condition is not systemic It is advisable to have a roengen examination of the chest and other structures that are liable to be involved, together with a complete neurologic examination and study of the spinal fluid The scar from a previous vaccination also shows early lesions of blastomycosis

DR ADRIAN SCOLTEN, Portland, Maine *Must one go out of the country to* acquire this disease?

A Case for Diagnosis (Erythroderma Ichthysiforme?) Presented by DR FREDERICK REISS

E G, an unmarried Puerto Rican woman aged 39, was admitted to the dermatologic service of Bellevue Hospital in October 1945 because of a generalized exfoliating erythroderma, which, however, did not include the mucous membranes The past history and the family history were not contributory There was no history of allergy, of ingestion of drugs or of any previous antisyphilitic therapy According to the patient, the eruption started on the face and neck about eight months previously and gradually spread over the entire body At the onset, blisters were present She had always lived in Puerto Rico until the fall of 1945

The patient has remained hospitalized up to the present During this period the clinical picture has been essentially unchanged except for the progressive development of generalized erythroderma and keratoderma, particularly of the palms and soles, and pronounced alopecia of the scalp During the first year of hospitalization there was a weight loss of 40 to 50 pounds (18 to 22 7 Kg), but during the past six months the weight has remained constant at approximately 80 pounds (36 3 Kg) The appetite has been good during the entire course There have been occasional febrile episodes, with the temperature rising to 102 to 103 F for twenty-four to forty-eight hours at a time

At present the skin over the entire body is erythematous and scaly The palms and soles present a decided keratoderma The nails are dystrophic, thickened and extremely brittle In addition, there are slight generalized lymphadenopathy and almost total alopecia

Reaction of the blood to the serologic test for syphilis was negative Repeated urinalyses showed a normal reaction A complete blood count revealed a hemoglobin content of 9 5 Gm, erythrocytes 3,520,000 and leukocytes 8,700, with 53 per cent polymorphonuclear leukocytes, 41 per cent lymphocytes and 6 per cent eosinophils Routine chemical examinations of the blood all gave essentially normal findings The basal metabolic rate was +36 per cent The reaction to the congo red test for the presence of amyloid was negative

Biopsy showed a nonspecific picture of acanthosis and hyperkeratosis

Additional laboratory investigations gave the following results The blood sugar was 92 mg per hundred cubic centimeters and the nonprotein nitrogen 27 mg The albumin-globulin ratio was 3 2 to 2 6 Gm per hundred cubic centimeters The blood chloride level (expressed as sodium chloride) was 456 mg per hundred cubic centimeters The serum cholesterol level was within normal limits The blood calcium was 10 4 mg per hundred cubic centimeters, and the serum potassium level was 16 2 mg The twenty-four hour urinary output of ketosteroids was 7 mg (normal, 10 to 15 mg)

DISCUSSION

DR FRED WISE It is possible that Dr Reiss' diagnosis is the correct one, but I believe the diagnosis of pemphigus vegetans should be entertained

DR FRANK C COMBES I have observed this patient for the better part of a year, as have other members of our staff I can well understand how, on looking at her for only a short time, Dr Wise might consider pemphigus However, this patient has never had any bullae, and at no time have we entertained this diagnosis I have never observed a dermatosis of exactly this nature Her palms are remarkable Here there is some erythema, but the most prominent feature is the hyperkeratosis, which is not that usually observed on the palms and soles It actually accentuates the normal cutaneous markings No topical therapy has succeeded in

DR JACOB H SWARTZ, Boston No It is named North American blastomycosis only to differentiate it from European blastomycosis

DR MAURICE J STRAUSS, New Haven, Conn *Is there any particular sulfonamide preparation which should be chosen?*

DR JACOB H SWARTZ, Boston I have had little experience in the use of sulfonamide drugs in treatment of blastomycosis, but several drugs of that group have been successfully used Iodides should not be used until after an intradermal test with blastomycin has been made It may be necessary to desensitize the patient before administering iodine compounds The same applies to patients with moniliasis

DR ALBERT LEVENSON, Bridgeport, Conn I should like to ask Dr Swartz whether the danger in giving sodium iodide is due to the fact that the patient has blastomycosis Sodium iodide is used in many conditions

DR JACOB H SWARTZ, Boston I believe that the form of iodide does not matter It is the allergic factor that counts The principle is the same as that in giving iodides to a patient with tuberculosis The reaction is on an allergic basis and may be compared to a Herxheimer reaction Any patient with a systemic fungus infection may be a poor risk

DR HARRY SIGEL, New Haven, Conn (by invitation) I saw several patients with blastomycosis of the skin in a military hospital, and all of them were treated with iodide without previous desensitization Though they were not previously tested for allergy to blastomycosis, none of those patients had ill effects

Pemphigus Erythematosus Presented by DR MAURICE J STRAUSS, New Haven, Conn

Foreign Body Granuloma in Skin of Finger Presented by DR E MYLES STANDISH, Hartford, Conn

Hidradenitis Suppurativa Presented by DR MAURICE J STRAUSS and (by invitation) DR CARTER MARSHALL, New Haven, Conn

Erythema Multiforme Presented by DR WILLIAM B SWARTS, Greenwich, Conn

Hemangioma of Left Thigh and Leg Presented by DR MAURICE J STRAUSS and (by invitation) DR HARRY SIGEL, New Haven, Conn

A Case for Diagnosis (Leishmaniasis of Skin?) Presented by DR ALBERT LEVENSON, Bridgeport, Conn

Tuberculosis Luposa Presented by DR MAURICE J STRAUSS, New Haven, Conn

Tuberculosis Luposa, Cutaneous Horn Presented by DR MAURICE J STRAUSS, New Haven, Conn

Bowen's Disease Presented by DR WILLIAM B SWARTS, Greenwich, Conn

eradicating this keratosis The odor which has been mentioned is that observed from other patients with hyperkeratosis and vegetative dermatosis and is due to putrefaction in the sulci and crevices

DR ISADORE ROSEN As far as erythroderma ichthysiforme is concerned, the clinical features do not fit in with that disease, which is almost invariably of congenital origin I am unable to make an absolute diagnosis, but I would suggest the possibility of Darier's disease

DR PAUL GROSS It would be interesting to hear about the therapy which this patient received during her year of hospitalization

DR FRANK C COMBS At one time we entertained the same idea as the chairman—that the patient might have Darier's disease, but this was ruled out on histologic grounds The patient has received large doses of vitamin A more or less empirically More recently, we have treated her according to the suggestion of Dr Goldzieher that this dermatosis was a manifestation of some endocrine disturbance occurring during the menopause I am sorry Dr Goldzieher is not here tonight, but Dr Reiss will be able to explain the therapy administered during the last two months, which I think is more logical than the previous treatment

DR PAUL GROSS There were two features which seemed important in this case One was the tongue, which had a magenta color and was rather smooth in appearance Secondly, there was pronounced anemia, which apparently has not changed to any degree during a year of therapy In other words, we are dealing with a case of generalized exfoliative erythroderma associated with lesions of the mucous membrane and profound anemia Such cases may respond to intensive therapy with vitamin B complex and particularly folic acid The fact that the patient is a Puerto Rican further suggests dietary deficiency, since we know that many of these people avoid meat in their diet If nutritional therapy is ineffective, the diagnosis of pemphigus foliaceus could be entertained This disease seems to be more common in South American countries than in the United States

DR FREDERICK REISS I have seen the patient only during the last two months I do not believe that I can offer a definite diagnosis, but since the onset of the disease was associated with bullae, Dr Wise's suggestion of pemphigus is a possibility I was led to think, however, that the disease process could be ichthysiform erythroderma, since the wet type starts with blisters We also have to recognize the other form, the dry type without blisters This case definitely began with blister formation, which later turned into erythroderma with plantar and palmar hyperkeratosis Hyperhidrosis is emphasized by Brocq and subsequent observers as occurring in erythroderma ichthysiforme, with, at times, loss of hair and sometimes increased growth of hair and nail plates I would not say that this case fits into the description altogether, because, as the chairman emphasized, in most instances the condition is hereditary Apart from that, there are many features suggestive of erythroderma ichthysiforme, and one may consider this a tardive form

An interesting symptom which I believe led us to the present therapy with estrogens was the amenorrhea which began six years ago, which may have some relationship with the disturbed keratinization I think the majority of French observers have emphasized endocrine deficiency, either ovarian, thyroid or adrenal This patient shows a definite endocrinopathy, not only clinically but biochemically, since there is tremendously decreased excretion of 17-ketosteroids The normal should be 11 to 15 mg, whereas she excretes only 7 mg All in all, I think that there is definite indication of an endocrine deficiency, but I cannot offer a definite diagnosis

Against the diagnosis of condyloma acuminatum are the hard consistency, the broad base and the smooth surface The unusual factor is that these cancers are of long duration without metastases to lymph nodes

Epidermodysplasia Verruciformis Presented by DR MARCUS R CARO and (by invitation) DR LAURENCE L PALITZ

B G, a white girl aged 16, first had cutaneous lesions on the wrists and ankles at the age of 10, with gradual extension to the present distribution There was some improvement each summer, but the lesions never disappeared, there were no subjective symptoms There was no history of parental consanguinity

On the dorsal surface of the hands are patches of erythematous, raised papules with verrucous surfaces On the left hand these papules extend across the outer side of the thumb to involve the volar surface of the thumb for a short distance On both hands they extend around the ulnar side of the wrists to the flexor surface and then along the ulnar part of the flexor surface of the forearms to the cubital fossae There is a diffuse patch of erythematous and slightly hyperkeratotic dermatitis about the right axilla and also on the inner surface of the right arm There are also diffuse lichenified patches on the outer surface of the hips, more on the right side, and on the outer surface of the right knee, while on the front of the left knee are many small warty papules On both insteps are many pea-sized, warty papules, which extend upward to the dorsal surface of the feet, across both ankles and along the outer side of the feet A few papules are present on the dorsal surface of several toes The skin is erythematous about the papules on the feet and ankles There is also diffuse acne on the forehead, which has improved with the use of 30 per cent sulfur paste The verrucous lesions have remained unchanged with local treatment and the administration of vitamin A and paraaminobenzoic acid

Histologic examination of a biopsy specimen from the left wrist showed a thick scale in which the cornified layers were interlaced Nuclei were absent except in one small area of parakeratosis The epidermis showed irregular acanthosis except for thinning beneath the parakeratotic scale At this site the granular layer was missing Elsewhere the granular layer was thickened, and in some cells there were small vacuoles The corium was edematous, and it contained a diffuse infiltration of lymphocytes, histiocytes and connective tissue cells In many places the edema and cellular infiltrate extended up into the epidermis, and the demarcation between the epidermis and corium became indistinct The Weigert stain showed the elastic fibers to be entirely missing from the upper part of the corium

DISCUSSION

DR HAMILTON MONTGOMERY, Rochester, Minn I would agree that this is an epidermodysplasia verruciformis clinically, but the histopathologic picture shows none of the features of this disorder, especially there is no evidence of vacuolization of the cells in the granular layer This histologic picture is more that of acrokeratosis of Hopf Histologically one might regard the condition also as a form of delayed epithelial nevus, using this term in the broadest sense

DR. MARCUS R CARO I think that clinically this case fits in essentially with the description of the disease in the literature Histologically it must be granted that there is here less vacuolization in the granular layer than has been described I recall also that in a patient shown before this society by Dr Weber (ARCH DERMAT & SYPH **49** 217, 1944) there was some variation from the classic picture I wonder whether we are not trying to classify the disease in these cases

on the basis of criteria that are a little bit too rigid I think that the lesions in all of these cases are forms of tardy epithelial nevi

A Case for Diagnosis Presented by DR FRANCIS E SENEAR

M S, a woman aged 75, was seen with an eruption on the arms and legs which had been present constantly for the past five years, without any appreciable change except for extension in recent years There are no symptoms The patient states that she was seen at the Billings Clinic some years ago and that a diagnosis of purpura was made She has been seen by a number of other physicians, and a variety of diagnoses have been suggested

Biopsy shows a slight degree of intracellular edema of the epidermis with liquefaction degeneration of the basal layer in several places At these sites the blood vessels were dilated and were surrounded by a loose infiltrate of lymphocytes and erythrocytes, some of the cells extending up to the basal layer Perl's prussian blue reaction did not show any iron pigment

A Case for Diagnosis (Idiopathic Multiple Hemorrhagic Sarcoma [Kaposi] or Pigmented Purpuric Lichenoid Dermatitis?) Presented by DR O H FOERSTER and DR H R FOERSTER and (by invitation) DR D M RUCH

V S, a man aged 28, is presented because of an eruption on his lower legs, feet and toes of three years' duration He stated that in 1944 the dorsal and lateral surfaces of his great toes showed a red-brown discoloration and elevated lesions The condition remained localized until January 1946, when it extended to the dorsal surfaces of his feet and toes and to the lateral surface of each ankle In June an apparent ulceration appeared on each side of his right ankle These open lesions healed in October 1946 The eruption was first observed on his lower legs in November 1946

Examination discloses a red-brown lichenoid, diffuse, small papular eruption in patches on the sides of the first three toes of the left foot and the first four toes on the right foot, the dorsal surfaces of the feet, at the bases of the toes the heels, ankles and the anterior and medial surfaces of the lower legs directly above the ankles

The result of the Rumple-Leeds test was negative Intradermal and subcutaneous tests with congo red elicited negative reactions for amyloid

The examination of the blood showed erythrocytes 6,530,000, leukocytes 12,750 hemoglobin over 18 Gm, thrombocytes 350,000, clot retraction time 1 hour and 20 minutes, coagulation time 10 minutes and 30 seconds and bleeding time 3 minutes and 30 seconds

The histologic examination of a section taken from the dorsal surface of the right foot adjacent to the toes showed moderate hyperkeratosis and a normal epidermis There was proliferation of the walls of all the vessels of the cutis A moderately dense lymphocytic infiltrate was present in the upper and middle parts of the cutis The iron stain showed a large amount of hemosiderin in the cutis

DISCUSSION

DR HAMILTON MONTGOMERY, Rochester, Minn In Foerster's case, it was difficult to make a histologic diagnosis The section showed proliferation of capillaries and some of the smaller venules Some of the capillaries were open ended, as one sees in Kaposi's sarcoma There were also apparently some lymphocytoid cells of Marchand Against a diagnosis of Kaposi's sarcoma was the diffuse uni-

A Case for Diagnosis (Erythema Bullosum? Pemphigus Vulgaris?) Presented by DR H VICTOR MENDELSOHN

A Case for Diagnosis (Macular Atrophy? Lymphogranuloma Venereum) Presented by DR FRANK C COMBES

Sarcoidosis Presented by DR H VICTOR MENDELSOHN

A Case for Diagnosis (Periarteritis Nodosa?). Presented by DR FRANK C COMBES

A D, a woman aged 35, was first admitted to the dermatologic wards at Bellevue Hospital in June 1946 presenting irregular, erythematous, urticarial lesions, widely scattered over the extremities and buttocks The lesions had first appeared approximately two weeks prior to this admission No previous history of asthma, hay fever, eczema, urticaria or other allergic manifestation was obtained Likewise, there was no family history of any allergic disorders

The eruption began with a few urticarial lesions on the thenar eminence of one hand, the wrist of the same hand and the buttocks The gradual appearance of similar lesions on the trunk and on other extremities was subsequently noted No pertinent past history was obtained The patient had undergone cholecystectomy in December 1944 for chronic cholecystitis and cholelithiasis She gave no history of having received any of the sulfonamide drugs

During July 1946, diffuse erythema, edema and doughy induration involving the left side of the face, the shoulder girdle, the upper part of the arms and the lower eyelids developed During the course of this episode, which lasted for almost one month, the patient became toxic and continued to run a temperature which ranged between 100 and 103 F Occasional vesiculobullous lesions appeared on the soles, the dorsa of the feet and the legs This acute picture disappeared gradually, and since the middle of August 1946 the patient has continued to show the present picture of a generalized, scattered urticarial eruption, with periods of exacerbation and partial remission

The urine has repeatedly shown traces of albumin and only occasional red blood cells Studies of renal function with phenolsulfonphthalein intravenously showed a 60 per cent excretion after two hours Repeated hemograms showed mild hypochromic anemia and constant eosinophilia, which has varied between 10 and 21 per cent

Examination of the stools showed no ova or parasites Intradermal tests for trichiniasis gave a delayed positive reaction after about twelve to nineteen hours Reactions to precipitin tests for trichiniasis were negative on two occasions Aspiration of sternal marrow revealed a normal picture Roentgenograms of the chest showed no infiltrations or other evidence of pathologic changes Roentgenograms of the skull and long bones revealed no abnormalities, and there was no evidence of calcification in the muscles Chemical examination of the blood showed no abnormalities with the exception of an increase in the serum cholesterol, which has ranged from 286 to 400 mg per hundred cubic centimeters

Biopsies of skin and muscle repeated on three occasions have failed to show any specific histologic picture The most recent biopsy of the skin, performed in November 1946, showed a diffuse vasculitis throughout the reticular layer of the corium and the subcutaneous tissue In addition, there appeared to be some proliferation of the intima and a granular degeneration of the walls of the involved vessels, with an accompanying pronounced perivascular infiltration which consisted for the most part of polymorphonuclear leukocytes and eosinophils

Almost the entire scalp is affected The skin presents a dull erythema, abundant scaling and crusting There are several small yellow crusts pierced by hair (scutula) and areas of atrophy with alopecia Hairs in the affected areas are dry, grayish and lusterless On the right thigh there is a small, round, erythematosquamous lesion with a minute yellow point in the center

On microscopic examination, hairs and crusts from the scalp contained Achorion schoenleini in abundance in the hair shaft and in scutula Scrapings from the focus on the right thigh showed one lanugo hair with the same fungi

The patient's mother was born in the United States Her father emigrated from Italy in 1920 There are two other children in the family A boy, aged 8, is free from infection In a girl, aged 2, a scaly lesion developed on the scalp two months ago Microscopic examination of hairs from this lesion showed fungi of favus



Fig 1—Favus of the scalp

DISCUSSION

Dr Marion B Sulzberger One must always bear favus in mind when seeing lesions of the scalp, even in patients of American birth. About twelve years ago I saw a telephone operator with favus of the scalp in mild form resembling dandruff or mild tinea amiantacea, with some involvement of several nails She was of American birth, and I do not think I would have thought of favus of the scalp if I had not examined the nails and recovered Achorion schoenleini She had been exchanging headpieces with the other girls at the telephone switchboard On questioning the mother of Dr Muskatblit's patient, I asked her if any members of the family showed signs of favus and she said there were none Then the girl herself volunteered the information that the father, who was born in Italy, had

DISCUSSION

DR GEORGE M LEWIS The features in this case, both clinical and histologic, may be interpreted to fit into the syndrome known as eosinophilic granuloma The lesions at present have undergone involution to a certain degree, and a biopsy taken at this stage might show a mixed infiltrate and not a pure eosinophilic infiltration The development of urticaria-like lesions, with subsequent disappearance and deposition of pigment, is a picture reminiscent of a patient I presented before this Section (ARCH DERMAT & SYPH **49** 375 [May] 1944), as well as before the Manhattan Dermatologic Society (ARCH DERMAT & SYPH **48** 436 [Oct] 1943) It is interesting that our patient had a Trichophyton purpureum infection of the feet, and, from the observations of Dr Cormia and myself, this case would seem to bear an etiologic relationship Inspection of this patient's feet suggested a fungous infection While not all cases of periarteritis nodosa are fatal, the prognosis is not as good as with eosinophilic granuloma, so that it would appear important to attempt to decide the diagnosis in this case by studying more histologic sections

DR CHARLES WOLF This case is unusual, and the diagnosis is difficult I was particularly impressed with a large lesion over the right pectoralis muscle which had a polycyclic border and was infiltrated There was severe itching The patient had had hemorrhagic bullae, papules, macules and all varieties of lesions that fit in with a diagnosis of mycosis fungoides I think that she bears watching for further evidence of that disease

DR FRANK C COMBES I appreciate Dr Lewis' remarks, and if a fungous infection and hyperergy can be substantiated in this patient they may explain the periarteritis The bullae seen on the feet tonight were not there a week ago She has had recurrent bullae, however, not only on the soles but on other parts of all extremities Examination of the walls and the contents of the lesions did not reveal fungi I do not know what the results of the trichophytin test were Periarteritis nodosa does not seem to be the rare disease originally described with a mortality in excess of 90 per cent In 1937 a comparatively benign chronic form was described (Carol, W L L, and Prakken, J R *Acta dermat-venereol* **18** 102-118 [Feb] 1937), and we have seen several patients recently who might be considered to have this type If the disease is interpreted as an allergic manifestation, it might be the result of a mycotic infection I do not know Sensitization to Bacillus coli has been indicated in some previous reports This patient underwent a cholecystectomy in 1944, which may bear on the origin of her present disease There was no histologic evidence of dermatomyositis but extensive nodal periarteritis throughout the reticular layer of the dermis and in the hypodermis, accompanied with a notable perivascular infiltration consisting essentially of polymorphonuclear cells and eosinophils The constant high eosinophil count of the blood, ranging from 10 to 20 per cent, is indicative of hyperallergization I am not prepared to say whether this patient has early eosinophilic granuloma, as I have never observed an early case of this disease

A Case for Diagnosis (Epidermolysis Bullosa?) Presented by DR EMANUEL MUSKATBLIT

Palmar and Plantar Keratoses (Arsenical?) Presented by DR MAURICE J COSTELLO

a deformed fingernail I think it would be worth investigating to find whether there is a focus there I hesitate to suggest any therapy on such scant evidence, but Dr Loeb at our clinic used a preparation called dermycin® (para-nitrophenol–sodium iodate solution) which had been submitted for trial He treated 1 patient with favus of the scalp which had recurred after two roentgen ray epilations

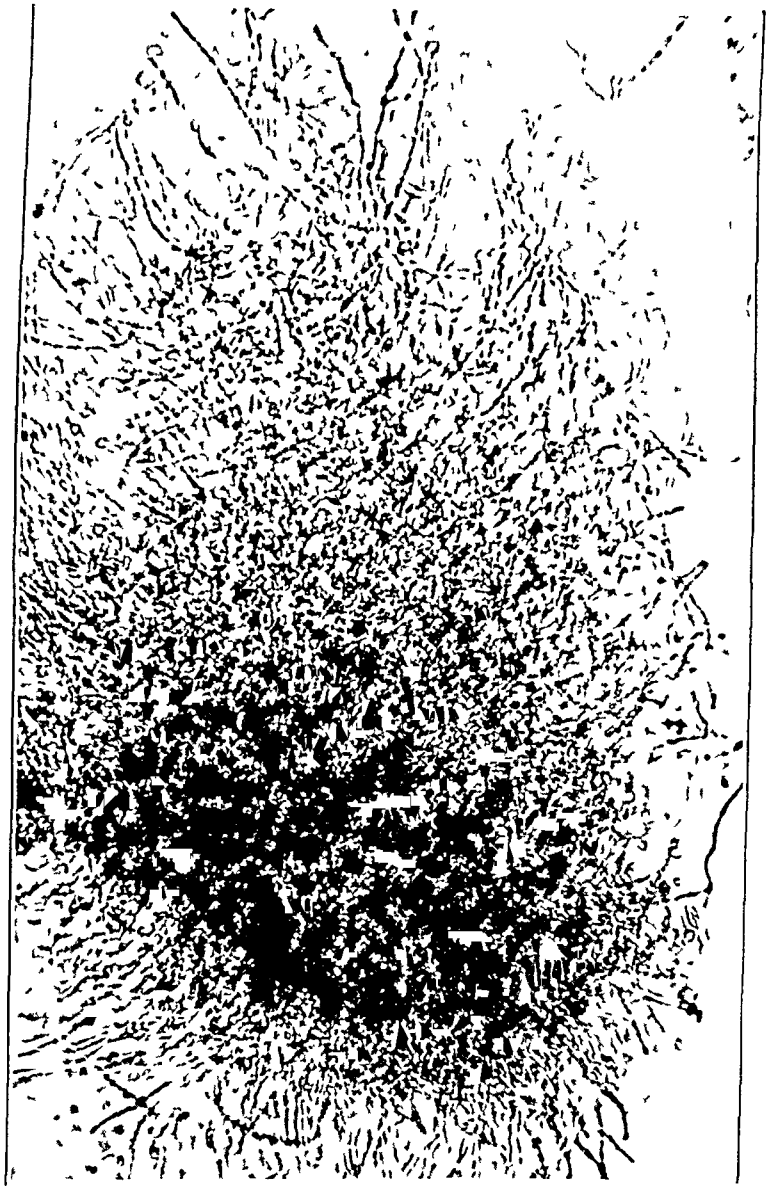


Fig 2—Achorion schoenleini in a scutulum from the scalp Potassium hydroxide preparation, × 300

with perfect results in a relatively short time Perhaps this preparation is worth trying in this case I shall be glad to see that Dr Muskatblit gets some dermycin® if he wishes to try it

Dr George M Lewis We had a patient a few years ago who had favus of the toe nail In the investigation of possible lesions in the family, the feet should

Trichophyton Violaceum Infection of the Scalp Presented by DR FREDERICK REISS

S G, a white boy aged 8, is presented from the Dermatologic Clinic of Bellevue Hospital with lesions of the scalp of four months' duration

Shortly after the patient's arrival from Greece about four months ago, small areas of alopecia were noted on the scalp These fluoresced poorly under the Wood light, and some patches had few, but noticeable, "black dots"

Potassium hydroxide preparation showed spores situated inside the hair shaft A culture on Oct 10, 1946, was sterile Culture on November 13 yielded Trichophyton violaceum

DISCUSSION

DR EMANUEL MUSKATBLIT This condition is relatively rare in the United States Such cases may escape attention when, as in this instance, there are few foci, probably a quarter of an inch (0 64 cm) in diameter, which do not show the typical broken hairs In such instances the condition may not be revealed by examination under the Wood light This case will probably require epilation with roentgen rays, and even with that the infection may not be easy to eradicate

DR GEORGE M LEWIS In Russia, Trichophyton violaceum is one of the common pathogens One of our recent visitors to this country confirmed that fact and showed me pictures of some of the generalized eruptions as well as of typical involvement of the scalp and nails I can attest to the difficulty of curing the patients They are apt to pass from clinic to clinic, they receive roentgen ray epilation in a clinic that performs epilation well, and then several foci will be found to have been left, and it is difficult to say how they escaped treatment Dr Fox, if he were here, would probably comment on a patient who had had three epilations It was a considerable time after the last epilation before the hair returned The condition finally cleared One must be careful, in considering roentgen ray epilation in these patients, to ascertain whether epilation has been done previously

DR FREDERICK REISS The point which Dr Lewis brought out about the wide dissemination of such cases in Russia is interesting, but there is another remarkable point In Russia, T violaceum was frequently the cause of a deep-seated inflammatory reaction, while this fungus according to our experience causes only superficial involvement

Extensive Pigmentary Changes Following Bismuth Therapy Presented by DR MAURICE J COSTELLO

Herman Sharlit, M D, *Chairman*

Maurice J Costello, M D, *Secretary*

Feb 4, 1947

Darier's Disease in Mother and Daughter Presented by DR SAMUEL M PECK

Granuloma Inguinale with Extragenital Lesion on the Cheek Presented by DR MAURICE J COSTELLO

DISCUSSION

DR MAURICE J COSTELLO It was interesting to note that this patient was presented at another dermatologic society the other night without a complete history, and the consensus of those present was that she might have scrofuloderma This

not be overlooked I believe that the patient should receive roentgen ray epilation without delay The longer the process is allowed to go on, the more danger of further dissemination Roentgen ray treatment would appear safe in this case, although I do not believe a patient should have a third epilation without careful consideration I doubt if local therapy is worth attempting, and I would be against experimentation when we know that local therapy is not effective When

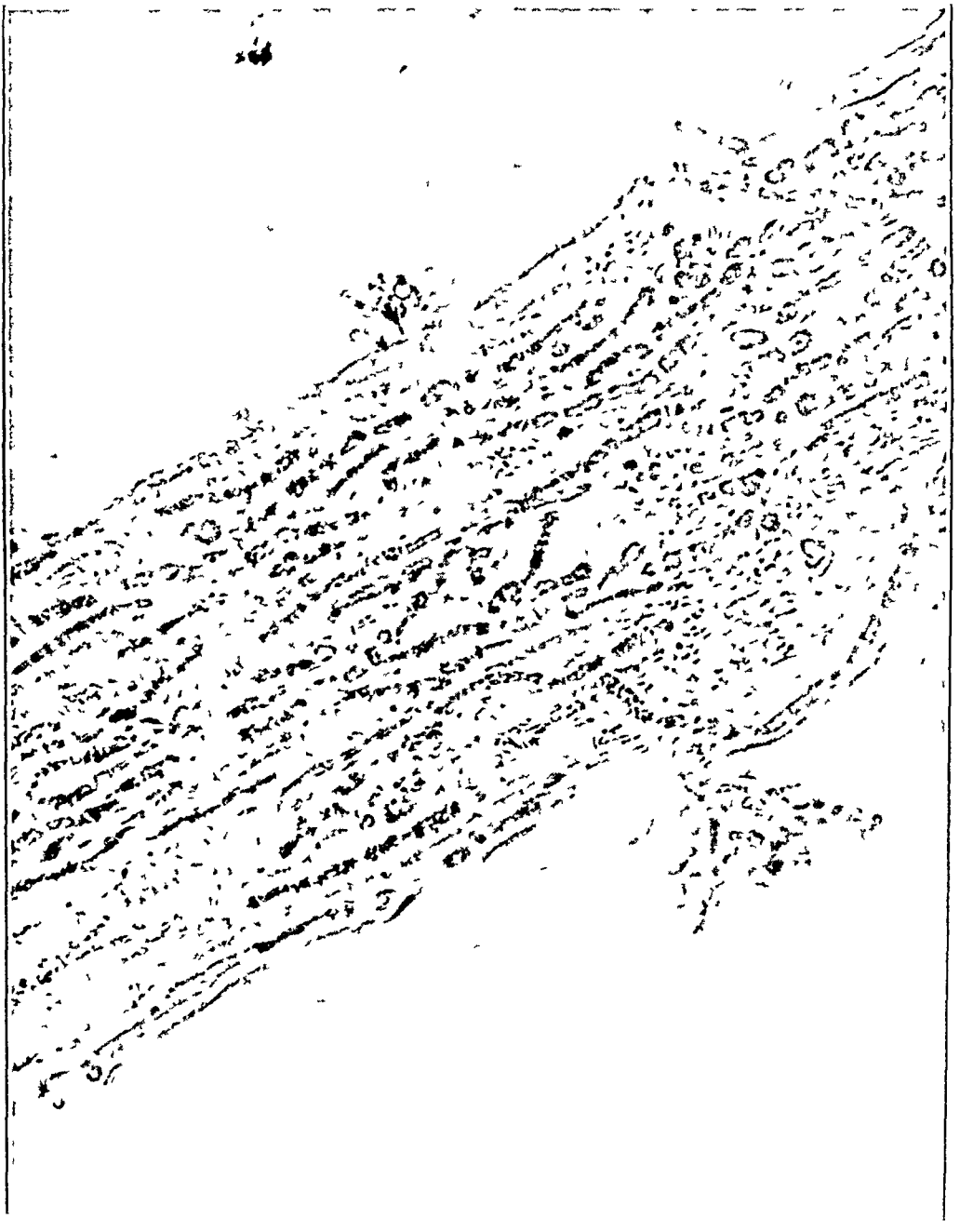


Fig 3—Achorion schoenleini in a lanugo hair from the thigh Potassium hydroxide preparation, × 770

I was examining this child, two of the younger men in the audience commented that they rather doubted the diagnosis because there were no scutula present I stated that we should censure Dr Muskatblit if the patient were presented with scutula The first step is to institute a good hygienic regimen to get rid of the bulk of crusts and scaling on the scalp before the roentgen rays are administered

confirms what Dr Chargin said, that one seldom if ever thinks of granuloma inguinale as having extragenital lesions, although I understand that the lesion in the first case ever described was extragenital I agree also with Dr Sobel I have seen several patients at Bellevue Hospital in whom the lesions began as enlarged inguinal lymph nodes, broke through the skin, and then took on the characteristics of granuloma inguinale in which Donovan bodies were found In this case Donovan bodies were found in the lesions on the neck and in the groin It would not surprise me if they could be found in the enlarged lymph node also, as suggested by Dr Bloom

A Case for Diagnosis (Lichen Planus) Presented by Dr William Leifer

Actinomycosis Simulating an Abscess Presented by Dr Emanuel Muskatblit

M A, a girl aged 17½, presents an inflammatory mass in the left mandibular area of three and a half months' duration The lesion is fluctuant and tender and discharges a grayish green, purulent material from its lower pole In October a decayed left lower molar was extracted Several weeks later a "lump" appeared which was believed to be an abscess This was incised and drained twice, with little evidence of healing The patient received ultraviolet irradiations for a while During the first week in January the cause of the disease was discovered when the granules in the pus were examined and the ray fungus of actinomycosis was seen in the fresh specimen as well as in the Gram stain Results of cultures have not yet been reported

To date the patient has received approximately 6,000,000 units of penicillin with noticeable improvement

DISCUSSION

Dr Nathan Sobel I was interested in the improvement with penicillin I understand that while penicillin is effective in most cases, some cases prove resistant to this form of therapy

Dr Emanuel Muskatblit The patient was hospitalized for a few days in one of the large hospitals, where the lesion was incised and drained, but it did not heal A few weeks later it was again incised and drained, and the patient was kept under observation for two and a half months, without any one's looking at a drop of pus under the microscope Regular surgical treatment did not have the regular effect, and there was a history of a bad tooth in addition

There is no scarring, no hardening and no typical sinuses It looks like an abscess It is confined to the skin and subcutaneous tissues, and there is no evidence of involvement of the deeper tissues Diagnosis from laboratory examination was surprisingly easy in this case Three weeks ago, every drop of pus, which could be obtained easily, showed the presence of granules which were visible in unstained preparations and also with the Gram stain The patient was given penicillin, 50,000 units every three hours, day and night 100,000 units per day She has now had 6,000,000 units or more During the last few days there has been considerable improvement The central area subsided and no more pus discharged—just a little serum and blood It is planned to continue until 10,000,000 units has been administered, and probably sulfadiazine and possibly potassium iodide will be given Roentgen therapy has been deferred because the dosage would have to be large, with high voltage, and because of the possibility of its producing radiodermatitis on the face

DR EMANUEL MUSKATBLIT The scalp should, of course, be cleaned with some desquamating preparation to dissolve all scales and crusts and the hairs cut short, almost level with the skin, before epilation If scales, crusts and long hairs are left, we will not get the roentgen rays close enough The suggestion to examine the family is excellent It is possible that the father has favus of the nails As far as Dr Sulzberger's remark about trying a new chemical is concerned, I agree with Dr Lewis It would be pretty hard to try a new chemical in such an extensive case I should like to try it on the patient's sister, who has only a small patch I agree that roentgen therapy is now perfectly safe if we know definitely that no more than eight subfractional doses were given

Pigmented Nevus, Melanosis Oculi Presented by DR BEATRICE M KESTEN

Sarcoidosis with Enlarged Auricular and Cervical Lymph Nodes in a White Woman Aged 22 Presented by DR PAUL GROSS

Incontinentia Pigmenti in a Girl Aged 13 Months Presented by DR HELEN CURTH

Calcinosis of the Foot and Elbow with Normal Amounts of Calcium and Phosphatase in the Blood Presented by DR HELEN O CURTH

A Case for Diagnosis (Leprosy? Syphilis?) Involving a Negro Woman from the West Indies Presented by DR A BENSON CANNON

Parapsoriasis Guttata Presented by DR F PHILIP LOWENFISH

A Case for Diagnosis (Melanoma of the Leg, Multicentric and Pigmented Basal Cell Epithelioma?) Presented by DR FRANK VERO

George M Lewis, M D, *Chairman*

Marion B Sulzberger, M D, *Secretary*

May 6, 1947

A Case for Diagnosis (Lupus Erythematosus? Erythema Solare?) Presented by DR MAURICE J COSTELLO

Lupus Vulgaris Improved from Treatment with Calciferol (Vitamin D_2) Presented by DR FRANCES PASCHER and DR JESSE A TOLMACH

Lichenoid and Miliary Sarcoid (Boeck) in a Negro Woman Improved After Treatment with Calciferol (Vitamin D_2) Presented by DR MAURICE J COSTELLO

DISCUSSION

DR MARION B SULZBERGER We have overwhelming evidence from many countries, including the United States, that calciferol should not be withheld in any case of sarcoidosis, scoruloderma, tuberculosis colliquativa or other tuberculoderm, unless it is contraindicated Many cases of sarcoid appear to respond well to this treatment, which lends some support to the theory that it is a form of

Superficial Epithelıomatosıs Presented by Dr S Irgang

C S, a white woman aged 55, is presented from Harlem Hospital with an asymptomatic eruption which was first noticed sixteen years ago This appeared as a single lesion on the left arm, followed two years later by another on the small of the back Other lesions developed slowly, so that at present they are on the back, left arm, left flank and face The majority of lesions on the right cheek are nevi

The eruption consists of dry, nonulcerated nodules and plaques The former are firm, smooth, elevated, mildly hyperpigmented and/or pinkish, glistening lesions varying in size from that of a pinhead to that of a split pea, while the latter consist of slightly infiltrated, superficial, well defined, pinkish or reddish, flat, slightly depressed, scaly lesions with pearly, threadlike borders and varying in size from that of a split pea to that of a dime Thirty-seven years ago the patient took orally a clear, liquid medication in drop dosage for nine months and again twenty-four years ago for a two week period On each occasion it was discontinued because of intolerance There are no cutaneous evidences of either arsenical hyperpigmentation or arsenical keratosis Histologic examination shows the typical picture of basal cell epithelioma

DISCUSSION

Dr David Bloom This patient gives a history of having received drops for acne vulgaris at the age of 18, administered during a period of eight months This was probably arsenic, and I suspect that her epitheliomatosis is a result of the arsenic ingestion

Dr Samuel M Peck We are not sure the patient received arsenic, and if one wishes to speculate on such a causal relationship, one would expect palmar and plantar keratoses A patient may take potassium arsenite solution (Fowler's solution) for no more than a few weeks or months, and twenty years later keratoses and epitheliomas may develop

Dr Herman Goodman Hundreds of thousands of persons have been given potassium arsenite solution in increasing dosage from 1 drop to 15 drops or more, three times daily, with no great number of them having superficial epitheliomas Pharmacologically, arsenic is a producer of keratin, it has been an ingredient in certain applications to the scalp as a hair grower Before the era of roentgen ray treatment for psoriasis, arsenic was given to patients with that disease In a few of them epithelioma developed on the site of the psoriatic patches A search of the literature disclosed that Arthur Alexander in 1920 assembled 18 patients with carcinoma of the skin together with psoriasis Of these, the disease in 11 was considered as malignant degeneration of arsenical hyperkeratosis or arsenical carcinomas on a psoriatic basis In the remaining 7 the lesions were considered as psoriatic carcinomas

Arsenic does foster the proliferation of epithelium, it is a keratoplastic agency It may cause the overgrowth of epithelium recognized clinically and under the microscope as epithelioma

Dr Samuel M Peck I still believe that one of the best therapeutic measures in the treatment of psoriasis is arsenic, given properly From the statistics of the incidence of epithelioma, one finds that most of the patients never received arsenic, unless food is a possible source Persons who have never been exposed to arsenic have just as much if not more epithelioma than those who have received moderate doses of potassium arsenite solution I do not mean that treatment should continue for twenty years Therefore, in presenting this case with arsenic as a possible

tuberculosis At the beginning we were careful to duplicate exactly the sterogyl 15® preparations used by Charpy and others, who emphasized that it was essential to give vitamin D_2 in alcoholic solution We now think this may not be necessary as our patients treated with ertron,® davitol,® etc, do as well as those given the alcoholic solutions The American preparations just mentioned are readily available here, whereas the alcoholic solutions are not

Follicular Atrophoderma of Body and Scalp, Chondrodystrophia Calcificans Congenita Presented by DR HELEN O CURTH

Lupus Vulgaris Successfully Treated with Calciferol (Vitamin D_2) Presented by Dr MAURICE J COSTELLO

Sarcoid of Boeck Presented by DR S IRGANG

Epithelioma Presented by DR MAURICE J COSTELLO

M G, a woman aged 84 from Lenox Hill Hospital, presents a "browsing" type of basal cell epithelioma involving the forehead, cheeks and nose It consists of nodular, waxy, shiny, ulcerating, infiltrated strands of epitheliomatous tissue involving these areas There is some distortion of the nose, especially in the region of the right ala nasi This patient has received an incredible amount of roentgen rays according to the Coutard technic to a number of the affected areas on the face during the past six years Because of the age and infirmity of the patient, the treatment has been palliative

DISCUSSION

DR CHARLES WOLF I wonder whether there was not a previous disease here, later developing into epithelioma, for example, syphilis, although her Wassermann reaction may be negative at present Epithelioma does not generally extend the way this one has It is of the ulcerative type when it becomes so extensive This has the clinical appearance of the morphea-like or scleroderma-like epithelioma which generally follows a previous disease

Dermatitis Herpetiformis (?) with Mucous Membrane Involvement and Nail Changes Presented by DR FRANCES PASCHER

P R, a woman aged 42, born in Puerto Rico, is presented from the New York Skin and Cancer Unit complaining of recurrent attacks of "blisters" on the body and in the mouth for the past year These lesions are preceded by burning and pain The patient denies the ingestion of drugs

The patient presents a multiform eruption on the trunk made up of erythematous macular and urticarial lesions varying in size and shape There are also some thin-walled bullae on a noninflammatory base, with gyrate patches of pigmentation, atrophy and scarring There is a hypertrophic scar on the right shoulder Bullae followed by superficial ulceration also appear on the lateral edges of the tongue and buccal mucosa, and leukokeratotic changes are seen in the mouth The Nikolsky sign is strongly positive The nail changes include thinning and separation of the nail plate and subungual hyperkeratosis The neurologic examination is entirely normal

Biopsy of one of the bullous lesions showed a bullous eruption, with no definite diagnosis possible, and no defect in the elastic tissue Reactions to potassium iodide and potassium bromide were inconclusive, since the skin separated with the least

causative agent, one should be cautious If, with the epitheliomas, there were typical hyperkeratoses on the palms and soles, and if, in addition, the patient had been taking potassium arsenite solution for many years, it would be more plausible to consider arsenic as a causative factor I would not hesitate to prescribe arsenic in lichen planus or psoriasis, because of the remote possibility of the development of epitheliomas Patients who have taken potassium arsenite solution for many, many years are those in whom keratoses and malignancy growths develop

DR MARION B SULZBERGER I do not agree with Dr Goodman that, because thousands of patients who take a drug have not had manifestations, the drug can be exonerated as a possible cause of trouble in a given case If that were a valid argument, one would conclude that the proved reactions from phenolphthalein, the barbiturates, antisyphilitic arsenicals, salicylates and the like were not due to those drugs because hundreds of thousands of persons have taken them with impunity I think it correct to start the other way around and ask how many persons with multiple benign epitheliomas have had therapy with arsenicals or exposure to arsenicals If one questions these patients carefully, one finds that a surprisingly large percentage have had exposure to inorganic arsenicals and an exceptional patient has had exposure to an organic arsenical The history of exposure in these cases is so high that it cannot be due to chance, so it is permissible to conclude that the lesions in some cases must be due in some way to arsenic I do not mean that all multiple superficial benign epitheliomas are due to arsenic But arsenic is not completely exonerated even in those cases without therapeutic exposure, because occult exposure is practically universal These lesions occur not only after larger amounts of the drug are given, but sometimes also after small amounts I agree with Dr Peck, on the other hand, that this is no reason for withholding a valuable drug Most of these conditions are benign, and the complications are rarely dangerous Moreover, the incidence of these disagreeable by-effects is very small, considering the large number of persons who have been exposed to arsenic Therefore, if arsenicals are valuable drugs, there is no reason for withholding them, provided that the indications are clearcut, even if it is established that benign epitheliomas are due to arsenic However, the dosage should be correct and no unnecessary risks taken Every patient receiving arsenic should be under constant medical supervision, and every prescription for arsenic should therefore be marked "no repeats"

DR DAVID BLOOM Years ago I presented from Bellevue Hospital the case of a woman who had received arsenic for psoriasis over a period of three years and in whom typical arsenical keratosis developed on the palms and soles with basal and prickle cell epitheliomas on the body

Granuloma Inguinale, Sickle Cell Anemia with Sickle Cell Ulcer of the Ankle Presented by DR SAMUEL M PECK

DISCUSSION

DR SAMUEL M PECK Here, instead of a thrombosed varicose vein and lack of a proper blood supply, there is actual thrombosis of a blood vessel due to sickle cell thrombi One of the methods of treatment I have tried which has resulted in fairly rapid improvement was keeping the patient in bed for months at a time, taking her blood serum and adding penicillin, and applying it locally as a dressing I allowed this to remain on for a period of four or five days before changing, and there was an amazing response, not only in the secondary infection as one would

trauma In three examinations of the blood the eosinophils did not exceed 10 per cent The bulla fluid was free of cells Results of serologic tests for syphilis were negative The urine was normal, and the basal metabolic rate was —11 per cent

Some improvement followed one course of treatment with potassium arsenite (Fowler's) solution, and a remission took place when therapy was discontinued Multiple vitamins have been taken three times daily over a period of months without apparent change Treatment with sulfapyridine is contemplated

DISCUSSION

DR FRANK VERO In spite of the biopsy, I think that a diagnosis of epidermolysis bullosa should be considered because of the nail changes, oral lesions and the atrophic changes and scarring on the back

DR DAVID BLOOM I believe that pemphigus should be considered, and onycholysis may be part of the eruption I do not recall having seen a case of dermatitis herpetiformis with such extensive eruption in the mouth

DR FRANCES PASCHER This patient presents a problem in differential diagnosis I do not know how one can say with finality what type of bullous eruption this might be, but I did consider all the bullous eruptions, such as epidermolysis bullosa, possible lichen planus and bullous Hansen's disease I considered the possibility of erythema multiforme bullosum, but this diagnosis was excluded because of the gyrate configuration of the patches, atrophy and pigmentation Most of the features fit in best with a diagnosis of dermatitis herpetiformis rather than the other eruptions

Hodgkin's Disease Treated with Nitrogen Mustard Presented by DR T J RIORDAN

E B, a man aged 20, is presented from St Vincent's Hospital In August 1945, there was enlargement of lymph nodes in the neck This was treated with roentgen rays In August 1946, a cluster of small papules appeared in the left axilla These persisted, grew progressively larger, coalesced and ulcerated Roentgen therapy had no effect In December, after nitrogen mustard therapy, the lesions regressed greatly In March 1947, the lesions again enlarged, reddened and drained Nitrogen mustard and roentgen therapy were again administered, and pronounced improvement followed, this has continued to date

DISCUSSION

DR A ROLLINO (by invitation) The usual cutaneous lesions observed in Hodgkin's disease are pigmentation, excoriations due to scratching and herpes zoster In a series of 75 cases of Hodgkin's disease my co-workers and I have encountered 3 patients with skin lesions similar to those demonstrated here, they appear in clusters of small nodules—in 2 cases on the chest and in the third in the axilla When the lesions first develop, they simulate pyoderma or a deep-seated vesicle They persist and may coalesce and ulcerate Biopsy establishes the diagnosis In the case demonstrated, roentgen therapy did not effect the lesion, but the response was spectacular to nitrogen mustard therapy The improvement lasted about three months, after which the lesions reappeared, grew larger and began to weep, itch and grow painful Again nitrogen mustard therapy was resorted to, and the lesions have almost cleared up

DR. DAVID BLOOM I should like to ask the presenter about the swellings of the right clavicle It seems to me there is involvement of the bone itself

expect, but in closure of the lesion Another feature is the pronounced anemia The patient was hospitalized mainly because of the very low blood cell count—as low as 30 per cent and often 50 per cent of normal

Eczema Verrucosum of the Legs Presented by DR LEWIS A GOLDBERGER

A Case for Diagnosis (Pemphigus? Bullous Eruption Due to Drugs?) Presented by DR LEWIS A GOLDBERGER

Multiple Benign Cystic Epithelioma Presented by DR S IRGANG

O D, an 8 year old Negro boy, has an eruption which was first noticed on both lower eyelids about a year ago The eruption is generalized, symmetric and nonpruritic and consists of pinpoint-sized to pinhead-sized firm, smooth, discrete, slightly elevated, flesh-colored and mildly hyperpigmented lesions, showing no tendency toward grouping The circular hyperpigmented area below the right jaw represents the end result of a recent fungous infection The child's mother has a similar eruption limited to both lower eyelids Histologic examination of lesions from the chest and right lower eyelid show the features of multiple benign cystic epithelioma

DISCUSSION

DR DAVID BLOOM Such lesions as the patient presents on his body are frequently seen in Negroes Recent histologic examination in such a case showed keratosis pilaris, mild keratosis extending also between the follicles However, the lesions on the face of this patient suggest the diagnosis as presented I am therefore inclined to consider that this patient has two kinds of lesions

DR NATHAN SOBEL I think that perhaps another pathologist would describe the eruption as syringoma, because that is closely related to benign cystic epithelioma and they may even simulate each other (Ingels, A E Epithelioma Adenoides Cysticum with Features of Syringoma, ARCH DERMAT & SYPH **32** 75 [July] 1935) It is the first case I have seen in a child I have seen a number of patients with the generalized syringoma type, but those I have seen occurred later in life, in the twenties or thirties

DR S IRGANG I agree with Dr Rosen that this disease is relatively rare in male subjects and it does not occur in so young a person Clinically, the lesions on the lower eyelids resembled multiple benign cystic epithelioma, but the others simulated micropapular tuberculid Histologically the lesions on the chest had to be differentiated from syringocystoma, but the latter was ruled out because the cells were evidently derived from the basal cell layer

Herman Sharlit, M D, *Chairman*

Maurice J Costello, M D, *Secretary*

March 4, 1947

Fixed Eruption Around the Mouth Due to Phenolphthalein or Bubble Gum? Presented by DR WILLIAM CURTH

DISCUSSION

DR WILLIAM CURTH There are various ingredients in bubble gum—cane sugar, corn sugar, cornstarch, a trace of vanillin, coumarone resin, oil of orange as a flavoring and oil of cinnamon, which is the main flavor Oil of cinnamon

DR A ROTTINO (by invitation) Yes, the clavicle is involved In no instance has the cutaneous involvement been primary, but it has been preceded by lymph node involvement The diagnosis in each case was established before the cutaneous lesions appeared

Kaposi's Sarcoma Presented by DR MAURICE J COSTELLO

A M, an Italian man aged 75, from the Lenox Hill Hospital Outpatient Department, in the early part of 1941 presented a soft, compressible, telangiectatic, marble-sized lesion on the right palm which was thought to be a pyogenic granuloma The lesion was destroyed by surgical diathermy but recurred with a number of satellite miniatures of the mother lesion Since that time numerous other lesions have appeared and are still present on the forearms, legs and thighs At present there are discrete, grouped, coalescing, purplish, globular, noncompressible, somewhat painful lesions on the legs and thighs, interfering to some extent with the venous circulation and causing brawny edema of the legs and feet There are a number of small warty excrescences on the dorsal aspect of the toes The axillary lymph nodes are enlarged Microscopic examination revealed the surface to be covered with stratified squamous epithelium surmounted by thick layers of keratinized, partially calcified material In a small area the surface epithelium was broken and missing Here and there exposed stroma showed fibroblastic proliferation and was rich in dilated small blood and lymph vessels A dense infiltration of inflammatory cells, chiefly round cells, was seen The electrocardiogram was normal

The disease has been well controlled with low, medium and high voltage roentgen rays The left palm received 1,000 r and the left axilla 1,200 r Two per cent sodium arsenate solution was administered by hypodermic injection at regular intervals, but was inferior to roentgen rays in therapeutic effect

DISCUSSION

DR DAVID BLOOM Two of my patients with Kaposi's sarcoma were treated with antireticular cytotoxic serum of Bogomolets but failed to respond

A Case for Diagnosis (Trophic Changes in the Legs and Feet Following Freezing) Presented by DR MAURICE J COSTELLO

Vaccination "Take," Left Index Finger Presented by DR TIMOTHY J RIORDAN

B D, a physician's office nurse, while assisting in numerous vaccinations two weeks ago, accidentally sustained a puncture wound from the virus capillary tube on the lateral aspect of the volar pad of the left index finger (fig 1)

Idiopathic Multiple Hemorrhagic Sarcoma (Kaposi) Presented by DR TIMOTHY J RIORDAN for DR ANTHONY ROTTINO

G M, a man aged 57, Italian, had Kaposi's disease for two and a half years Pathologic examination of a mass in the pharynx, lingual and tonsil area, removed in November 1946, and a biopsy of a cutaneous lesion, corroborated the diagnosis Treatment with seventy injections of nitrogen mustard was ineffectual

The patient was critically ill on admission to St Vincent's Hospital on Feb 25 1947, with evidence of ascites, gastrointestinal hemorrhage and peripheral

has caused cheilitis in some cases, but there is no case on record of pigmentation or fixed eruption due to oil of cinnamon

Pemphigus Erythematosus (Senear-Usher Syndrome) Treated with Vitamin A, Erythroplasia of Queyrat *Presented by* DR FRANK VERO

J W, a Russian Jew aged 73, is presented from the Vanderbilt Clinic with an eruption on the face, trunk and extremities of sixteen months' duration and a lesion on the penis which has been present for five years

In 1944, after an attack of hematuria, a diagnosis of papillary carcinoma of the bladder was made It was treated by fulguration, and there has been no recurrence since September 1944 At that time a penile lesion was discovered, which had been present since 1942 This affected the glans, corona and sulcus

Late in 1945 small vesicles appeared on the sternum and quickly ruptured From then on, new lesions have appeared on the chest, arms, back and abdomen, and six months ago they spread to his face These lesions ruptured spontaneously, and soon became covered with a rather heavy, greasy scale He experienced little pruritus He denied the use of any drugs

Examination on admission showed dull erythematous patches, varying from 3 to 7 5 cm in diameter Intact bullae were present, these were about 1 cm in diameter and flaccid Most of the lesions were covered with gray-brown, greasy scales which were readily separable Heavy crusting was most apparent on the back and chest Two weeks later the small lesions on the right cheek had spread to cover both cheeks in butterfly shape A positive Nikolsky sign was elicited at this time on the patient's back On the glans penis, extending to the sulcus, there was a well defined, dull red, eroded and infiltrated lesion, measuring 1 5 by 2 cm, with a leukoplakic patch near the frenulum praeputii

A blood cell count showed 13 0 Gm of hemoglobin, 4,810,000 red blood cells and 5,500 white blood cells, with 68 polymorphonuclear leukocytes, 31 lymphocytes and 1 eosinophil

The serum cholesterol was 300 mg per hundred cubic centimeters and the serum protein 7 2 mg The albumin was 5 0 mg per hundred cubic centimeters, globulin 2 0 mg and nonprotein nitrogen 33 mg The cephalin flocculation test gave a negative reaction

Biopsy of material from the upper region of the right arm revealed a moderately acanthotic and edematous epidermis, with fairly prominent rete pegs in the central portion but with a flattened cutiepithelial line of juncture elsewhere No bullae or vesicles were seen in the section, but in their central portions were seen areas suggesting the "corps ronds," "grains" and space formation similar to those seen in Darier's disease, Hailey and Hailey's benign pemphigoid and pemphigus foliaceous The corium was edematous, particularly in the region of the pars papillaris, the capillary vessels were engorged and surrounded by a considerable perivascular infiltrate of round cells In view of the clinical picture, it was felt that a diagnosis of pemphigus erythematosus was justified

Biopsy of material from the prepuce showed an elongated, rectangular piece of tissue composed of loosely bound, fibromatous bundles, numerous blood vessels and lymphatic vessels and mucosa which presented a number of interesting changes in several areas There was an infiltration with lymphocytes, plasma cells and round cells in the subcutaneous tissues throughout their entire length, but it was most pronounced wherever the epithelium was thickened In such places the infiltration was massive The capillaries were numerous Where the epidermis was thickened there was also dyskeratosis The stratum granulosum was indistinct The most notable change was in the prickle cell layer Here the cells



Fig 1.—Vaccination "take" on the index finger

appeared fused, with absence of intercellular bridges The nuclei were pale and irregular, but they were hyperchromic There was considerable edema Some cells were large and vacuolated, and in one area were seen cells resembling Paget cells The infiltration with lymphocytes was pronounced The basal layer was indistinct Mitosis was present

Potassium permanganate baths were prescribed Sulfapyridine, 0 5 Gm four times daily, was taken from October 1 to November 6 A slight improvement was noted after one week of treatment, but it then ceased Carbarsone, 0 25 Gm four times daily, was given from November 6 to December 8, with questionable improvement The administration of vitamin A, 200,000 units daily, was begun on December 4 and has continued up to the present, and vitamins in the form of a therapeutic formula have also been taken during this period By Jan 15, 1947, there was remarkable improvement of the lesions, and by February 10 only the pigmented residua were found

The patient refused surgical therapy for the penile lesion

DISCUSSION

Dr Beatrice M Kesten Tonight I think it would be difficult to confirm the diagnosis, but when we saw the patient in December it was one of the most typical examples of the Senear-Usher syndrome that we have encountered

Dr Fred Wise The concurrence of two different types of dermatosis in this patient is of particular interest The eruption on the trunk appears to conform to the Senear-Usher dermatosis, and the diagnosis of erythroplasia of the penis has been confirmed by the microscopic examination It is of course interesting to speculate on the possible pathogenic relation between the two eruptions

Dr Gerald F Machacek This patient was shown by me last October, and at that time there was present a typical Senear-Usher syndrome The lesions of the body followed the neoplastic lesion on the penis In fact, he had another neoplasm, for which he has been operated on several times—a papillary carcinoma of the bladder, with presumptive cure The histologic picture of the penile lesion was epithelioma in situ The other lesions at that time were typical

Dr J Gardner Hopkins I think Dr Vero was interested in presenting this case because of the patient's response to treatment We cannot be sure that the result is due to the treatment given, but the change in the appearance of this man has been striking It came after a course of carbarsone during which he had shown no visible improvement Dr Vero employed this particular therapy because of the more evident response to vitamin A in a somewhat similar case

Dr Frank Vero I cannot explain the rationale of vitamin A therapy and the result obtained I treated another patient with pemphigus (Senear-Usher type), a 76 year old patient who had had the disease for three years She had had day and night nurses and all kinds of therapy including penicillin, bismuth, iodides and vitamins, without results or with only a temporary improvement In September 1946 she had keratoderma of the feet and subungual hyperkeratosis I prescribed 100,000 units of vitamin A daily, and within three to four weeks all her lesions healed The patient is able to go out daily She has gained weight, and for the past two months my services have not been needed It is interesting that this patient has had a poor appetite all her life, so that her food had to be actually forced on her

edema Roentgen examinations revealed intraluminal masses and obstruction On March 17 operation was performed in an attempt to relieve the obstruction and control the hemorrhage The patient died five days later

A Case for Diagnosis (Keratosis Blenorrhagica? Psoriasis?) Presented by DR MARION B SULZBERGER for CAPT C D BELL and DR LIONEL RUBIN

F G, a white man aged 22, first became ill in September 1946 At this time severe pain developed in the right hip, without apparent cause, which forced the patient to stop work This was shortly followed by similar pain in the right shoulder and scapular areas and on both sides of the chest He was then acutely ill, his temperature rising as high as 101 F in the afternoon The smaller joints of the extremities, including the wrists and ankles, also became painful In October the right great toe nail became tender and elevated, accompanied by pain and swelling of the dorsum of the foot The toe nail was removed by an osteopath, with no improvement At the same time the patient had iritis of the right eye, and he was now so ill that he was admitted to the United States Naval Hospital, St Albans N Y He had lost 30 pounds (14 Kg)

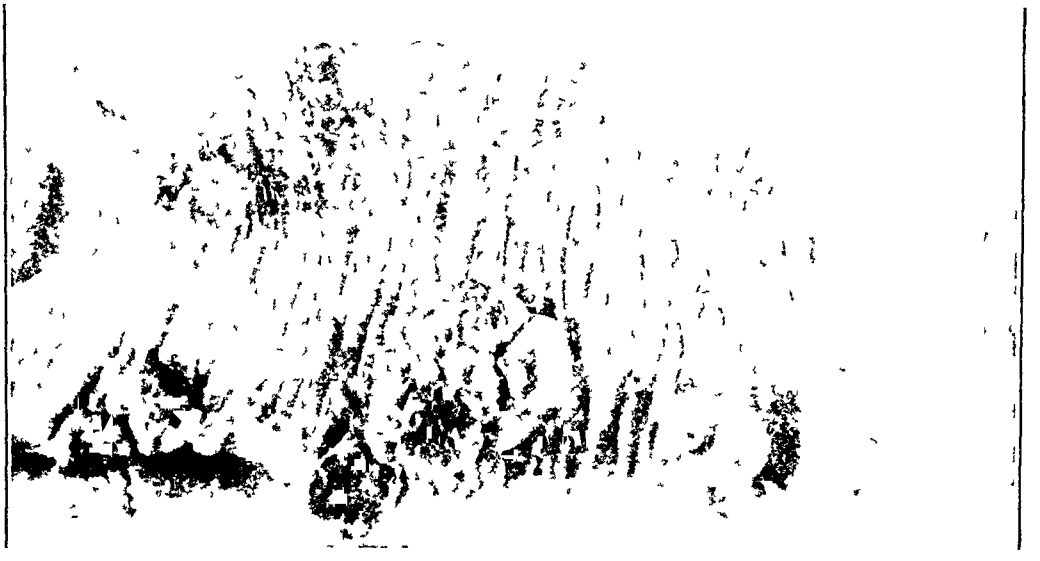


Fig 2—Gross pathologic specimen of intestinal section

The admission examination on November 18 revealed a dilated right pupil with posterior synechial pigment deposits on the lens and a cloudy aqueous blurring the fundus There were erosions on the tongue, buccal mucosa and palate and there was a discrete, papular eruption of the skin of the genitalia and inner aspect of the thighs "resembling scabies" The right scapula, left wrist, lumbar spine, right hip and right ankle were tender on pressure and painful on motion but exhibited no local heat, redness or swelling It was also noted that there was "an infected right great toe with associated cellulitis of the right foot" Otherwise the results of physical examination was normal, and, as the impression was that he had acute rheumatic fever, he was assigned to the medical service The erythrocyte sedimentation rate was 22 mm per hour, white blood cells 12,500 with polymorphonuclear leukocytes 73 per cent and lymphocytes 20 per cent, red blood cells, 4,300,000 and hemoglobin 12 5 Gm Blood cultures were negative

While on the medical service the patient continued to have a spiking afternoon temperature varying from 99 to 101 F The iritis cleared slowly with treatment, although some permanent dilatation of the pupil remained He received 6

A Case for Diagnosis (Keratosis Pilaris? Lichen Scrofulosorum?) Presented by Dr F Philip Lowenfish

A Case for Diagnosis (Hemangiopericytoma?) Presented by Dr George C Andrews

J J M, an American student aged 18, first noticed a small "pimple" just inside his left naris about one year ago This tumor has continued to grow and is painless About five weeks ago his physician punctured the mass with a needle, which caused it to bleed a great deal

A single pea-sized, moderately firm, erythematous cystic nodule is present just within the left nasal orifice on the medial anterior aspect

The Wassermann reaction of the blood was negative, and the blood count was normal Biopsy has not yet been performed

DISCUSSION

Dr Charles Wolf These banal lesions are deceptive at times, the most innocent-looking lesions have turned out to be highly malignant In this case, I am of the opinion that it is a benign lesion I would favor granuloma pyogenicum

Dr Gerald F Machacek *On the clinical basis, I agree with the diagnosis* It is a site where hemangiopericytomas frequently occur Definite diagnosis must await examination of biopsy material

Dr Fred Wise The location and clinical appearance are in favor of the diagnosis of hemangiopericytoma A young boy seen at the Skin and Cancer Unit had a lentil-sized, slightly elevated, pinkish papule on the middle of the upper lip After complete desiccation it recurred and a tumor formed, spreading peripherally and into the deeper tissues It required an extensive radical operation on the upper lip, which I believe was performed by Dr Arthur Purdy Stout

Leprosy (Tuberculoid Type) in a Puerto Rican Man Aged 72 Presented by Dr A Benson Cannon for Dr Charles Lincoln

A Case for Diagnosis (Multiple Keloids? Dermatofibrosarcoma Protuberans [*Hoffmann*]?) *Presented by Dr George C Andrews*

Favus of the Scalp and Glabrous Skin Presented by Dr Emanuel Muskatblit

V V, a white girl aged 13, born in the United States and living in Belleville, N J, is presented from the New York University Skin Clinic

The disease of the scalp began four years ago with a scaly lesion which was diagnosed as psoriasis and treated with various ointments, ultraviolet irradiation and roentgen rays (eight roentgen ray treatments were given at weekly intervals from June to September 1946) The disease proved resistant to treatment and gradually progressed until it reached the present state During these four years the hairs from the scalp have been examined six times, and it has been reported each time that they did not show fungi The patient also had several red and scaly lesions on various parts of the body These lesions disappeared without treatment *Only one focus, on the right thigh, has persisted for the last two months*

Gm of sulfadiazine daily for two weeks, followed by 6,000,000 units of penicillin intramuscularly, and boiled milk, but joint pain persisted and the cutaneous eruption gradually progressed He was first seen in consultation on the dermatologic service early in December, at which time a diagnosis of keratosis blenorrhagica was suggested and it was recommended that an investigation be made for a probable prostatic focus A genitourinary consultation disclosed no urethral discharge, shreds in the second specimen of a two glass test and a slightly boggy but not remarkably enlarged prostate, the secretion of which exhibited 50 white blood cells per high power field The patient consistently denied gonorrhea by name and symptoms He was given weekly prostatic massage and diathermy, and in January the urine was free of sediment and he had recovered from acute conjunctivitis of the left eye However, fever, tachycardia and joint pain persisted, with involvement of the right wrist and shoulder, onycholysis of all nails with hyperkeratosis of the bed and gradual extension of the skin eruption On Jan 11, 1947, the patient was seen in consultation by Dr Sulzberger, who suggested the possibility of an atypical psoriasis, the patient was transferred to the dermatologic service

The patient then received daily starch baths to macerate the heavy corneous lesions, followed by application of 50 per cent salicylic acid in petrolatum The fever, tachycardia and arthropathy continued unchanged, while a severe secondary anemia was now evident, the hemoglobin was 11 Gm, red blood cells 3,200,000, and white blood cells 8,200, with polymorphonuclear leukocytes 67, lymphocytes 25 and eosinophils 6 per cent Small transfusions of 250 cc of whole blood were administered with improvement

Biopsy revealed pronounced parakeratosis and acanthosis, migrating leukocytes in the rete processes and a heavy cellular infiltrate in the upper third of the corium The papillae were greatly elongated with thinning of the suprapapillary plates while the rete pegs were thickened, clubbed and fused These observations were felt to be consistent either with keratosis blenorrhagica or with psoriasis

The patient continued to show erosive lesions of the tongue and palate, but no vesicles were ever seen The original eruption on the genitalia had subsided, but on the lower extremities the lesions had tended to coalesce to form indurated, erythematous plaques in which the original papules could be distinguished The trunk, forearms, upper arms, nose and scalp were now involved by the process, and close study revealed that new lesions appeared first as apparent vesicles, perceptibly hard, which became pustular (cloudy) in about four days and then commenced to exhibit a tan, heaped-up, tenacious and hard crust The corneous exudate appeared to project through the skin, its base being surrounded by a slight erythematous halo Where formerly these hornlike excrescences had remained intact, they now yielded to the action of baths and salicylic acid and desquamated, leaving dime-sized, bright red papules These papules tended to coalesce to form the plaques previously described on the ankles

Prostatic secretion continued to show many pus cells Ointments of 10 per cent crude coal tar and 5 per cent ammoniated mercury had no effect, and the patient was then given bismuth sodium triglycollamate by mouth, beginning January 25, with 1 tablet (75 mg of bismuth) three times daily and increasing to 2 tablets (150 mg of bismuth) three times daily for a total equivalent of 9 7 Gm of bismuth No effect whatever was obtained On February 27 he was given potassium arsenite (Fowler's) solution by mouth, treatment commencing with 4 drops three times daily, gradually increasing to 7 drops three times daily and then decreasing to 4 drops again, for a total of 20 3 cc over a period of nineteen days Again no effect was evident

form staining of the entire section with hemosiderin rather than a spotted deposition of hemosiderin There was no evidence of any tumor stage, such as fibrosarcoma I believe that this is probably an early stage of Kaposi's sarcoma both clinically and histologically One must bear in mind that Kaposi's sarcoma can progress slowly, just as mycosis fungoides may remain in an early plaque stage simulating parapsoriasis for a period of many years

DR STEPHEN ROTHMAN The patient presented by Dr Senear was seen in the University of Chicago Clinics by Dr Stenhouse and myself in 1943 At that time the tentative clinical diagnosis of Majocchi's disease with hypertension was made The biopsy specimen did not show extravasation of blood or blood pigment I believe that the eruption has not changed much in the last four years, and it is remarkable that the hypertension, too, is rather benign and stationary

Gottron in Germany stressed the point that Majocchi's purpura is always associated with either polycythemia or hypertension I do not know whether this has ever been confirmed, but the association of a widespread telangiectatic eruption with hypertension certainly is remarkable

DR F E SENEAR Several years ago I observed 2 cases, 1 patient was shown before this society and originally presented the somewhat mammalated appearance that this patient showed on the leg Histologically the lesions in both cases were typical of Kaposi's sarcoma

DR HARRY R FOERSTER, Milwaukee In our case we had considered the possibilities of Kaposi's idiopathic hemorrhagic sarcoma, amyloid disease and lichenoid pigmentary dermatosis and, on clinical grounds, decided in favor of the last named Dr Montgomery made a histologic diagnosis of Kaposi's sarcoma without having seen the patient MacKee and Cipollaro reported a case of Kaposi's sarcoma in which only inflammatory manifestations were present, which is in accord with Dr Webster's comment I am inclined to agree with him Our patient observed his first lesions three years ago These lesions were confined to the feet, particularly the dorsa of the toes, for almost three years In January 1946, the eruption extended to the dorsum of each foot and to the ankles, and during the last five or six months lesions have appeared on the legs Today he shows lesions that have developed since our first examination of him six weeks ago These lesions are more of a purpuric type The dark red in this case contrasts with the orange in Dr Caro's case, which I thought was an example of Schamberg's disease In Schamberg's or Majocchi's disease I have not seen the papular infiltrate exhibited by our patient, nor have I seen a case of Kaposi's sarcoma with so little infiltration I therefore favored a diagnosis of pigmented purpuric lichenoid dermatitis

Extensive Morphea Presented by DR S ROTHMAN and (by invitation) DR L RUBIN

Eosinophilic Granuloma Progress with High Voltage Roentgen Therapy Presented (by invitation) by DR M PIERCE and DR S ROTHMAN

Since this patient was presented originally at the Chicago Dermatological Society, in February 1947, further search for a positive agent in cultures from biopsy specimens, inoculation into guinea pigs and on bacteriologic mediums have failed to reveal the presence of an organism

On February 28, a biopsy of the skull lesion in the right parietal bone was made The histologic picture of this lesion was similar to that found in the granulomatous lymph node tissue The microscopic report was as follows The

tissue fragments were made up for the most part of large acidophilic or nonfoamy macrophages These had large irregular-shaped nuclei with indistinct nucleoli They contained a moderate amount of cytoplasm Many of these macrophages were binucleated, and there was some infolding of the nuclear membrane Scattered among these cells were a moderate number of eosinophils, more numerous in some of the fragments There were also a few smaller cells with dark nuclei, which presumably were lymphocytes There were a few multinucleated giant cells, some of these containing vacuoles or slitlike spaces A stain for fat (sudan IV) revealed that a moderate number of the macrophages contained small or moderate-sized fat droplets, or lipoprotein granules, most of which were not anisotropic Blood lipid studies showed no elevation of the total blood lipids or blood cholesterols

Therapy consisted of external irradiation, massage and physical therapy to correct the fibrosis in the cervical region Before admission to Bobs Roberts Hospital, the child had received a total of 2,593 r between Jan 13, 1939 and June 12, 1945 Since June 14, she has received forty-three treatments to seventeen cutaneous lesions, totaling 1500 r with single doses of 300 to 500 r She has experienced no radiation sickness She improved progressively The lesions are gradually regressing, and at present there are no discharging areas She has gained 27 to 30 Kg in weight since admission The retraction of her head has improved to some degree The patient is now to be discharged from the hospital and will be followed in the outpatient department

Eosinophilic Granuloma Presented by DR EDWARD A OLIVER and (by invitation) DR E LORANT

M E C, a white man aged 42, was presented at the March meeting He is presented today to show the effect of treatment

DISCUSSION

DR H M BULEY, Champaign, Ill (by invitation) These 2 cases illustrate again that there are various etiologic entities in eosinophilic granuloma In both cases there is symptomatic involvement which would not be present in many other cases The improvement following roentgen ray treatment is remarkable In the case I observed roentgen rays had no effect I saw the patient two weeks ago, and the lesions were practically as I saw them two years ago

DR ASHTON L WELSH, Cincinnati (by invitation) I wish to report further on the patient that my co-workers and I observed in Cincinnati, who was treated in the same fashion as this one His improvement was as striking as was the improvement in Dr Oliver's patient He now has fewer lesions, has gained weight and is considerably improved His spleen, which was palpable before roentgen therapy was begun, is still palpable but decidedly smaller The few small palpable lymph nodes that he had before roentgen therapy are still palpable and have been only slightly reduced in size They were chiefly around the neck and in one axilla We have been carefully watching this man, and I cannot help feeling that this syndrome is a little different from other forms of lymphoblastoma, if it is a lymphoblastoma, particularly in that the toxic or "id" reactions in this syndrome are so pronounced Low voltage roentgen rays administered to various skin areas in the man we treated produced little change, as in Dr Oliver's case

DR HAMILTON MONTGOMERY, Rochester, Minn Eosinophilic granulomas of the skin should be differentiated from eosinophilic granulomas of the skin and bone A series of articles appeared in the February 1947 issue of THE ARCHIVES Eosinophilic granuloma of the skin may be of various types, including pseudo

At this point, Dr Lionel Rubin, consultant, suggested the use of estrogenic substance On April 3, diethylstilbestrol therapy was begun, he was given 0 5 mg daily, which was increased to 1 5 mg daily At the end of two weeks no new lesions were appearing and former lesions on the trunk were evident only as pigmented macules The mouth was clear Painful gynecomastia necessitated reduction of the dose of diethylstilbestrol to 1 0 mg daily on April 18 Improvement continued rapidly with respect to the cutaneous eruption, but no improvement of the arthritis was noticeable Roentgen reexamination on May 2 showed extensive demineralization of all osseous structures visualized, narrowing of involved joint spaces due to cartilaginous destruction and varying degrees of flexion and extension deformity Comparison of these roentgenograms with those of December 1946 revealed a fulminating type of rheumatoid arthritis

At present the patient exhibits loss of all finger nails, with hyperkeratosis of the nail bed, and an erythematous plaque on the dorsum of the right foot, which is slightly infiltrated The joint deformities persist in the fingers and toes, but the large joints are much less painful and motion is greater The patient has lost 70 pounds (32 Kg) during his illness Since April 17, the afternoon temperature has been less than 100 F

DISCUSSION

Dr E T Bernstein I think that the disease in this case is arthropathia psoriatica It seems to me that the nails and skin showed lesions of that disease

Dr Emory Ladany (by invitation) This case does not impress me as one of keratosis blenorrhagica for the following reasons In keratosis blenorrhagica there is gonorrhea This patient denies gonorrhea, and prostatic smear and cultures were negative It may be arthropathic psoriasis Since 1920, keratosis blenorrhagica has frequently been confused with arthropathic psoriasis In keratosis blenorrhagica, a urethral discharge precedes the arthritis, which is followed by the cutaneous lesions In arthropathic psoriasis there are first cutaneous lesions and then joint lesions In keratosis blenorrhagica the large joints are usually the ones involved and there is no distortion There may be a few cases with ankylosis of the involved joints, but this is rarely so Usually the arthritis is evanescent, whereas in arthropathic psoriasis the small joints are usually attacked and ankylosis and deformities are common The other diagnostic possibility is Reiter's disease, which has also been mixed up with keratosis blenorrhagica in the last decade or so This is a urethritis which is nonspecific, with arthritis and nonspecific conjunctivitis Ocular lesions are also common in keratosis blenorrhagica, and they have been reported exceptionally in arthropathic psoriasis Out of 47 cases of Reiter's disease reported, in only 13 were there cutaneous lesions, but without such great deformities of the nails and joints as in this case I reviewed 166 cases of keratosis blenorrhagica and also dealt with the differential diagnostic points of the two other diseases, and I believe that the disease in this case is arthropathic psoriasis

Capt C D Bell (by invitation) About a month ago this man's appearance was different than it is today At that time there was a generalized eruption, of which one now sees evidence in the form of pigmented macules on the trunk and upper extremities This was characterized as a vesiculopustule These lesions developed day after day, they started as vesicles, became pustular and then hyperkeratotic It is true that there is no gonorrhea On the other hand, the prostatic smear even today was loaded with pus cells, so that I think that there is fair evidence that at some time the patient did have a urinary disorder

and shoulders Vesicular encrusted lesions in plaques are seen in arciform arrangement with active borders and clearing center The old lesions seem to have left depigmented areas The Nikolsky sign can be elicited near the lesions

Results of serologic tests for syphilis were negative, the urine was normal, and no fungi could be found in scrapings The report of biopsy by Dr Charles Sims was Hailey-Hailey disease

The patient is married and has no children He does not know whether either of his parents or his brother or sister had a similar condition

DISCUSSION

DR ARTHUR B HYMAN It was suggested that this might be tertiary syphilis because of the configuration of the lesions, but they are crusted and bullous and there is a positive Nikolsky sign There is some clinical similarity to dermatitis herpetiformis, but the eruption does not itch The patient said that he has had it for six years The unusual feature is the fact that, if his story is correct, the eruption developed at the age of 67 No cases have been reported in which the disease developed as late as that Most cases are familial, but such a history was not elicited from this man His parents died years ago, and his siblings live far away, so that he would not know about the state of their skin Fortunately, the histologic picture in Hailey-Hailey disease is characteristic

DR GERALD F MACHACEK I treated a patient with a similar condition, and the patient improved with large doses of vitamin A, the improvement lasting over a period of months I do not know the ultimate outcome

As a matter of fact, the problem is older than when the Haileys posed it McCarty, in his "Histopathology of Skin Disease," wrote of these peculiar cases which have some characteristics of pemphigus and some of Darier's disease

DR WILBERT SACHS I was surprised to hear Dr Hyman call this Hailey-Hailey disease In our article my co-workers and I decided that this is a variant of epidermolysis bullosa

DR ARTHUR B HYMAN (by invitation) Whether it be epidermolysis bullosa or not, this eruption was described by Hailey and Hailey, and therefore there is no discrepancy

The lesions in Hailey-Hailey disease are found on the sides of the neck, axillas and groins with a degree of symmetry, and there is usually a familial history The disease lasts many years with frequent remissions One can generally exclude other possibilities, such as tinea by mycologic examination, syphilis and other diseases, by careful analysis of history, lesions and symptoms The histologic aspect of this disease is characteristic, and the only other eruption for which it could be mistaken at a quick glance under the microscope is Darier's disease, but in the latter one always finds corps ronds and grains In Hailey-Hailey's disease the lacunas are characteristic and are found just above the basal cell layer, corps rond are not found, and grains are rare

Sarcoid, with Results of Kveim Test Presented by DR JESSE A TOLMACH

E L, an Italian woman aged 39, is presented from the New York Skin and Cancer Unit with an eruption of six years' duration Nearly the entire scalp is involved with scaly erythematous flat patches Around the right ear and toward the back of the neck there are several pea-sized papules of light yellow-orange On the left side of the face, right arm and right thigh there are indurated telangiectatic coin-sized plaques The past history is not relevant

DR LIONEL C RUBIN (by invitation) This patient gives no history of gonorrhea, but, as Dr Bell stated, he has chronic prostatitis, before studies for bacteria were made he had already received 5,000,000 units of penicillin, so that may have prevented isolation of the Gonococcus In this case the joint changes preceded the cutaneous eruption by months In psoriasis it is the reverse Also, the cutaneous lesions were originally vesicles and pustules, becoming hyperkeratotic, of the waxy type, which is characteristic of keratosis blenorrhagica, and he had lesions in the mouth He has a history of iritis That would be difficult to fit in with psoriasis, but it would fit in well with gonorrhea He had a severe constitutional reaction, with pronounced loss of weight and a swinging temperature Why was there no response to penicillin? Such cases have been reported in the literature, and I think that Dr Ladany's patient had positive evidence of gonorrheal urethritis, yet the rash and joint pains did not respond to penicillin therapy There has been great improvement in the last two weeks I do not know whether that is coincidental or whether it was due to the diethylstilbestrol therapy Every type of therapy had previously been tried without improvement, and diethylstilbestrol was suggested because of the rarity of this condition in female subjects After the patient had received diethylstilbestrol, gynecomastia developed, he began to improve, and practically all the cutaneous lesions disappeared

DR LOUIS TULIPAN I believe that this is a case of psoriasis arthropathica In this disease hyperkeratotic lesions are prone to develop, especially on the palms and soles, plus pronounced subungual keratosis In gonorrheal arthritis one expects a monarticular involvement This man has a multiarticular involvement He has a generalized eruption on the body, which coincides with a superficial type of psoriasis, and shows fairly typical plaques I do not believe that arthropathic psoriasis can be ruled out simply because the arthritis preceded the eruption, or vice versa I feel that it is a case of psoriasis arthropathica

DR WILLIAM CURTH Was a complement fixation test for gonorrhea performed?

DR RUDOLPH L BAER Besides the complement fixation test for gonorrhea, it might be worth while to try a new procedure recently described, which might help to differentiate the present eruption from Reiter's disease In the Scandinavian literature (Storm-Mathisen, A *Acta dermat-venereol* **26** 547, 1946) is described a skin test for Reiter's disease using as test material tissue emulsions and joint exudate from a patient with "known" Reiter's disease

DR LOUIS TULIPAN I would also suggest that this man might have received medication for his arthritis—one of the sulfonamide drugs or some other drug—and that the vesicular-pustular eruption which developed all over the body may have been a reaction to that or to the penicillin Such eruptions frequently terminate in the guttate or nummular form of psoriasis

DR MARION B SULZBERGER The discussion shows that this is still a case for diagnosis I would put arthropathic psoriasis first with a question mark, keratosis blenorrhagica with two question marks second and Reiter's disease with three question marks third I have seen 3 cases almost identical to this one, and the same discussion followed in each instance One thing was not mentioned In the one biopsy, the histologic picture was characteristic of psoriasis The patient is beginning to improve since receiving diethylstilbestrol Dr Rubin is to be complimented Even though it is not yet certain that this estrogen has cured the patient, it would surely be well worth while to treat other patients with that preparation The similar case Dr Baer and I reported and depicted (Sulzberger, M B, and Baer, R L Yearbook of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc 1944, pp 202-203) terminated fatally

Results of serologic tests for syphilis were negative The urine and blood cell count were normal The tuberculin reaction was negative in a dilution of 1 100 A roentgenogram of the chest showed perhaps slight engorgement of the superior great vessels There was a slight degree of lymphoid nodulation at the hilus and root devoid of definite etiologic characteristics There was moderate generalized hypervascularity No evidence of recent parenchymatous infiltration was seen The report of biopsy was sarcoid The result of the Kveim test was negative after nine days, with the Oslo antigen With the Copenhagen antigen it appeared to be 1 plus after three days and 1 to 2 plus after seven days

DISCUSSION

DR DAVID BLOOM The patient shows typical sarcoid lesions on the back of the neck, but the other lesions are flat and not infiltrated Together with the lesions on the scalp, they form an extraordinary feature in this case

Sporotrichosis Presented by DR TIMOTHY J RIORDAN

H W, a white man aged 50, born in the United States, is presented from St Vincent's Hospital The patient worked for two months repacking novelities shipped from Mexico in what is called "Mexican hay" In reshipping, this "hay" is mixed with excelsior On Jan 7, 1947, a thorn of cactus pricked the right middle finger The patient said that when he pulled out the thorn at least half an inch (1 cm) had been embedded under the nail plate He applied iodine Three days later he complained of a red, painful swelling He was cared for by a surgeon, and after four days of wet dressings the infected area was incised and

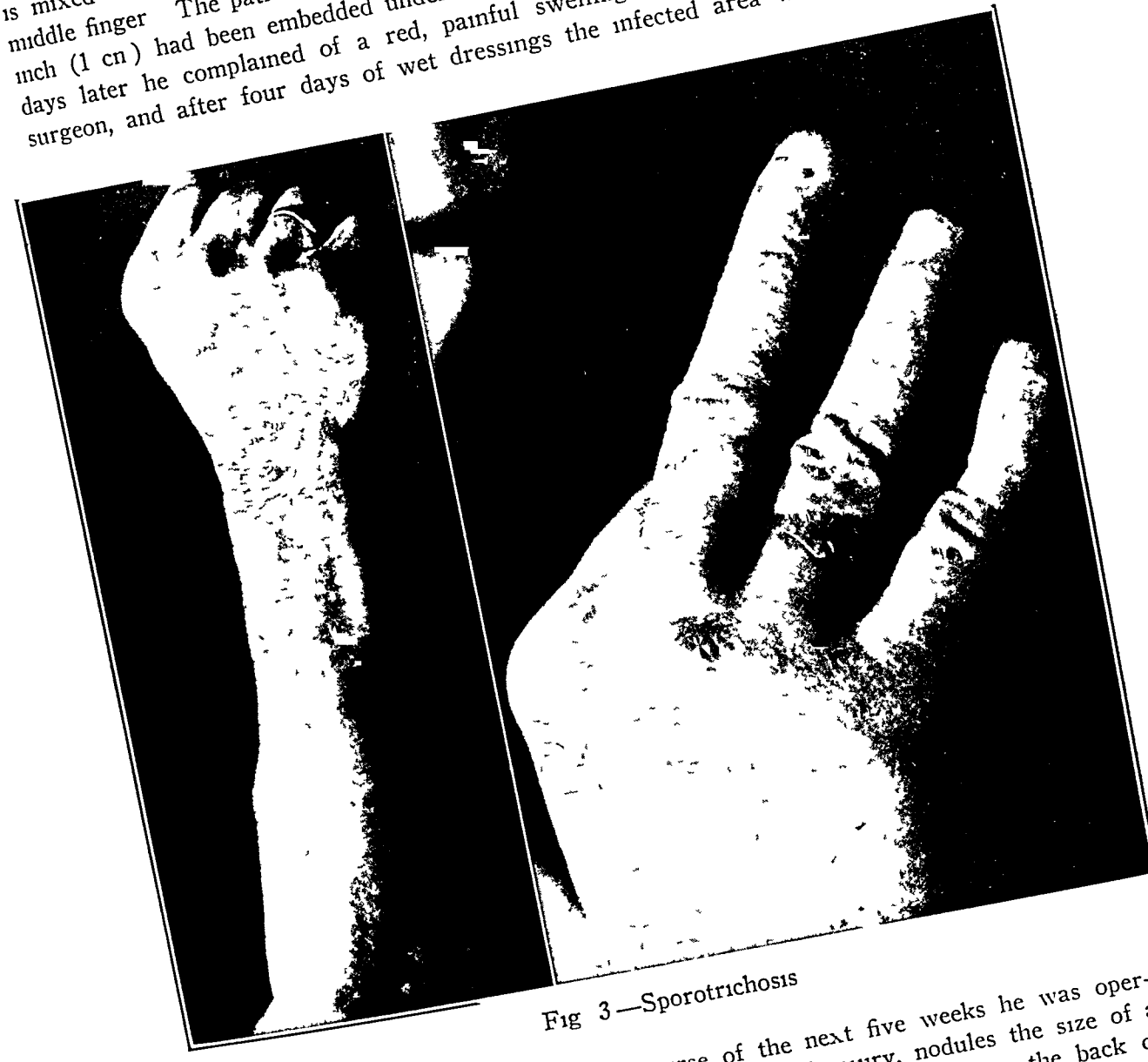


Fig 3—Sporotrichosis

the nail partially removed In the course of the next five weeks he was operated on four times Seven weeks after the date of injury, nodules the size of a pea and larger appeared, extending from the distal phalanx across the back of the hand and forearm to above the elbow These nodules were in linear arrangement, apparently following the course of the lymphatics They were dusky and firm, and subsequently one or two broke down Microscopic examination of the material discharged failed to reveal evidence of fungi Cultures from the nodules were positive, corroborating the diagnosis It is important to note that there was no enlargement of the epitrochlear or axillary lymph nodes Prior to the spread of the infection penicillin therapy was used without effect

NEW YORK DERMATOLOGICAL SOCIETY

George C Andrews, M D, *President*

George M Lewis, M D, *Secretary*

March 26, 1946

Axillary Hidradenitis Suppurativa, Pyoderma, Cystic Acne in a Girl Aged 15 Presented by Dr Fred Wise

Nevus Cerebriformis Presented by Dr Fred Wise

B G, a single girl aged 18, in good general health, presented a birthmark involving the skin of the posterior and external lateral surfaces of the right thigh It extended from the gluteal fold down to about one third the length of the thigh, it was roughly rounded in outline, with well defined borders and was approximately 8 inches (20 cm) in diameter In addition to the primary growth, there were a few scattered satellite, pea-sized nodules at a distance from the main lesion The tumor consisted of groups of soft, light brown, partly pedunculated and partly sessile nodules, some of which exhibited cerebriform and cauliflower-like surfaces, while others consisted of yellowish white, rounded, easily compressible "lumps" resembling superficial deposits of fatty tissue, covered with clinically normal skin

The birthmark produced a pronounced degree of disfigurement of the affected region, the patient was presented for the purpose of obtaining advise as to therapy

DISCUSSION

Dr. Howard Fox I would do nothing at all for this lesion It is fortunate that it is not situated on the face, neck or arms To perform an extensive skin graft would be ridiculous, as the lesion does not bother the patient in the slightest degree

Dr. Eugene F Traub The lesion in this case is too extensive in my opinion for surgical intervention Furthermore, since the lesion is a spreading and extending one, I feel sure that it would certainly promptly appear beyond the line of surgical excision This in itself would be most distressing to the patient and would, in my opinion, argue against surgical removal Superficial desiccation, on the other hand, could be carried out on each of the lesions, and, because of the large amount of intervening skin between the patches, this would strike me as being the treatment of choice Microscopic examination of one of the lesions would prove that this is probably a benign type of growth, and, if the desiccation is carried out properly, it could be done with safety and great improvement to the patient

Dr A Benson Cannon I agree with Dr Fox This lesion should be untreated, but, should treatment be demanded, it might be possible to remove the lesion in successive steps, leaving only a linear scar eventually

Dr. George M MacKee I suggest leaving the lesion alone, or else complete excision, with plastic repair I know of several instances in which epithelioma developed in this variety of nevus after it had been severely traumatized with solid carbon dioxide

The patient was given sodium iodide, 1 Gm daily the first week and every other day thereafter, with potassium iodide by mouth He has responded well, and eruption is almost clear, but there is still evidence of nail changes and residual nodules are present on the forearm

This is the first compensation case of sporotrichosis in the state of New York

NOTE —One year later the patient was completely cured

George M Lewis, M D, *Chairman*

Marion B Sulzberger, M D, Secretary

Nov 5, 1947

Follicular Lymphoblastoma Presented by DR FRANCES PASCHER

H R, a man aged 44, complains of lymphadenopathy of three years' duration A node was excised for histologic examination from the right axillary chain two years ago There has been no palpable change in the size or consistency of the nodes during the three months in which the patient has been under observation A red patch appeared near the left temple one year ago A few weeks later a similar lesion appeared near the right temple The patient has lost about 10 pounds (4 5 Kg) during the past three years He has been well enough to work but does not feel as energetic as formerly

There is a well defined plaque of erythema and infiltration in both preauricular areas The nodes in all superficial chains are enlarged The liver and spleen are not palpable

A biopsy specimen was taken from the right temple on August 8 The section showed masses of cells not surrounded by any inflammatory exudate The collagen fibers within the lesion were edematous and broken The cellular exudate consisted of small round cells containing highly pigmented nucleoli There were no eosinophils or mitotic multinucleated cells The diagnosis was lymphoblastoma

The section taken from the lymph node was examined by Dr M Richter, and the diagnosis was malignant lymphoma, follicular type

A roentgenogram of the chest revealed no abnormalities Scout roentgenograms of the abdomen showed a slightly prominent liver and spleen Study of the sternal marrow was attempted, but a suitable specimen could not be obtained Three complete blood counts were normal, as were the results of urinalysis The Wassermann reaction of the blood was negative

DISCUSSION

DR DAVID BLOOM Years ago I saw all the patients for whom this diagnosis was made at Bellevue Hospital All the patients showed universal erythroderma with pronounced enlargement of the lymph nodes This patient shows only a few circumscribed cutaneous lesions in association with generalized adenopathy The diagnosis as presented should therefore be questioned

DR GERALD F MACHACEK I have seen several patients without erythroderma and without glandular involvement—1 with the lesions localized, 1 more diffuse and both of them evidently cured by total excision Reexcision was necessary for 1 a year after the first operation, but ultimately the entire disease process was eliminated and the patient cured

DR MAURICE J COSTELLO I should like to confirm what Dr Bloom said, that all patients observed during the time Dr Symmers was making his studies of this disease had generalized or universal erythroderma I cannot recall a case in which the eruption was limited to a small area I think that the patient must have

Universal Scaling Erythroderma Presented by DR HOWARD FOX

Lichen Sclerosis et Atrophicus, Accompanied with a Bullous Eruption Involving Vitiliginous Areas of the Vulva and Anus Presented by DR MAURICE J COSTELLO

Dermatitis Herpetiformis Refractory to Treatment with Sulfonamide Drugs Presented by DR MAURICE J COSTELLO

Nevus Pigmentosus et Pilosus Presented by DR ANTHONY C CIPOLLARO

D W, aged 2 months, was first seen on March 21, 1946, because of an extensive nevus involving the major portion of the body The father and mother have no similar lesions, and there is one other child in the family, who is well The pediatrician informed the parents of the possibility of cancer developing in these lesions and of the possibility that the child may grow up with mental defects

The patient now presents a lesion which is black and thick, and involves the bathing trunk area and halfway up the trunk There is hair in all parts of the lesion On other portions of the body are isolated black or brown pigmented hairy lesions

DISCUSSION

DR HOWARD FOX This case of bathing trunk nevus is not the typical brown hairy type The pigment is rather dark, almost black, and, in addition, there are other defects There is nothing that can be done for this child

DR A BENSON CANNON I believe that this is a benign type of lesion

DR EUGENE F TRAUB There are two types of nevi present in this case One, an ordinary brownish black, pigmented lesion with some slight fine downy hair, and the other, a deeper-seated bluish black or slate black mass It is possible, therefore, that there are a blue nevus and an associate nevus of another type, possibly a junction To further complicate the picture, there are some nodular masses underlying several of the bluish lesions, and they may be part of the bluish nevus, or they may perhaps represent areas of subcutaneous fat necrosis of the newborn The child is just a few months old, and the masses have been present since directly after birth As subcutaneous fat necrosis of the newborn is a self-limited process and usually clears up in a month or two, keeping this patient under observation will settle the diagnosis without the need of a biopsy

DR FRED WISE Is it the consensus of the members that the nevus be untreated?

DR HOWARD FOX None of the patients with subcutaneous fat necrosis that I have studied had pigmentation like this, and there always was a definite hardness which this child does not have In subcutaneous fat necrosis of the newborn, the skin is practically normal in color The location of the disease is also different from that in this patient

DR MAURICE J COSTELLO I think that the masses represent the fibrolipomas rather frequently observed in this type of pigmented hairy nevus I agree with Dr Fox that there is nothing in these tumors to suggest subcutaneous fat

enlargement of the mediastinal nodes, because dilatation of the superficial cutaneous veins was a prominent feature, producing a caput medusae effect

DR WILBERT SACHS The patients that I have seen had not only generalized erythroderma but also severe itching Any such extensive eruption associated with prolonged itching may give a similar picture Some believe that the constant scratching results in the enlarged lymph nodes and that Symmers' disease is not an entity per se

DR EUGENE F TRAUB I am not sure whether the history stated whether the other lymphoblastomas, such as leukemia and mycosis fungoides, had been excluded, as the nodules in this case seem unusually firm I, too, have had the experience of seeing only generalized erythroderma in patients with this microscopic picture and have followed 1 case for approximately fifteen years, during which the patient had about three severe exacerbations and then the disease cleared up as a result of local therapy only It seemed to me that in these cases the lymph node involvement was secondary to that of the skin, but that does not seem to be the case in this patient, in whom the lymph nodes enlarged before the cutaneous lesions appeared Perhaps the presenter can tell us what has been done to exclude the other types of lymphoblastomas

DR ELSE A BARTHEL The condition in the biopsy specimen of the skin definitely resembled leukemia rather than a lymphoblastoma The appearance of the biopsy specimen of the lymph node was that of a lymphoblastoma Since the node reactions offer more of a diagnostic picture than the skin, it was thought preferable to accept the diagnosis based on the pathologic changes in the lymph node

DR FRANCES PASCHER The concept of giant follicular lymphadenopathy, or Brill-Symmers' disease, is still in an evolutionary phase It is now regarded by Craver and others at Memorial Hospital as "an early setting for lymphosarcoma" rather than a disease entity In 1938 Symmers pointed out that in some cases of universal chronic erythroderma there is local or general enlargement of the superficial lymph nodes with the histologic characteristic of giant follicular lymphadenopathy Similar histologic changes in the lymph nodes have also been described in association with other dermatoses Hurwitt *(J Invest Dermat, 1942)* stated that the benign follicular hyperplasia in the lymph nodes associated with dermatoses differs definitely from that in follicular lymphoblastoma He designated this benign follicular hyperplasia as dermatopathic lymphadenitis Differential diagnoses can be made only after careful study

My impression is that the patient presented has a follicular lymphoblastoma which has developed into a lymphosarcoma with cutaneous metastases The mediastinal nodes are not enlarged, and the blood cell count is normal

(NOTE—A lymph node was later excised, and the histologic report was lymphosarcoma)

Postvaccinal Erythema Multiforme Bullosum? Epidermolysis Bullosa? Presented by DR JOSEPH L MORSE

Multiple Superficial Basal Cell Epitheliomas Presented by DR JOSEPH L MORSE

M H, a woman aged 65, is presented from the Skin and Cancer Unit with a history of having taken potassium arsenite solution (Fowler's solution) at intervals for many years for the treatment of "eczema" The lesions first developed about thirty-five years ago, and since then new ones have continued to appear Many were treated years ago at the Vanderbilt Clinic with roentgen rays and radium

necrosis of the newborn The duration and age of the patient is against it A malignant melanoma may develop in this infant

DR ANTHONY C CIPOLLARO I do not believe that there is any fatty necrosis here I do not believe that this shows any lipomatous tissue I think that it is a mass of nevus cells I feel, as do most of us here, that the lesion should not be treated and that nothing can be done for the child, I agree with Dr Cannon that it is a relatively benign type of lesion

Mycosis Fungoides. Presented by DR FRED WISE

Chronic Lichenoid Discoid Dermatitis, Arrested; Dermatophytosis, Erythroplasia Presented by DR A BENSON CANNON

Universal Scaling Erythroderma Presented by DR HOWARD FOX

L S, a man aged 62, a dress shop owner, first noticed an eruption ten years ago It began on his legs and within six years had become universal The eruption is red, scaly, dry and nonpruritic In each axilla there are two partly fused, firm lymph nodes, the size of a pigeon's egg and a hen's egg, respectively

Laboratory examinations showed a faint trace of albumin in the urine The Kline and Mazzini reactions of the blood were negative A blood examination on Nov 10, 1944, showed 6,500 leukocytes, with 52 per cent polymorphonuclear neutrophils, 44 per cent lymphocytes and 2 per cent eosinophils A second blood examination, on March 7, 1946, showed essentially normal observations, except for 12 per cent monocytes

A biopsy specimen taken on Feb 1, 1946, was examined by Dr Wilbert Sachs, who made a microscopic diagnosis of tuberculosis cutis His report was as follows Throughout the middle and upper parts of the cutis there is a diffuse intense cellular infiltration composed of wandering connective tissue cells, small round cells, occasional plasma cells and many epithelial giant cells, the latter arranged in tubercle formation The overlying epidermis is irregularly acanthotic Part of the basal cell margin is washed out and part is intact There is some parakeratosis No lepra organisms were found

Four years ago, and again one year ago, the patient was operated on for inguinal hernia, on each occasion by a different surgeon Both operations were failures and were followed by large elephantiasic masses in the upper third of the thighs On one of these occasions, an inguinal (or femoral?) node was excised and examined microscopically It was said to have shown nonspecific adenitis

The patient appeared to be in fairly good general health He never takes drugs, including vitamins He has had a good deal of roentgen treatment without any benefit, which would tend to exclude either psoriasis or mycosis fungoides

DISCUSSION

DR FRED WISE Generalized tuberculous erythroderma was described by Jadassohn (Volk, R Tuberkulose der Haut, in Jadassohn, I Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927 vol 10, pt 1, p 420)

The patient now has several discrete crusted lesions on the forehead, sides of the cheeks, back and abdomen and small superficial erythematous macules scattered on the trunk and extremities There are several whitish atrophic scars and telangiectatic atrophic areas on the forehead, cheeks, abdomen and thighs Numerous keratoses are present on the back and abdomen The palms and soles are free of lesions

A report of biopsy of a lesion on the abdomen was basal cell epithelioma

Multiple Superficial Basal Cell Epitheliomas with Arsenical Keratoses

Presented by Dr Jack Wolf

C B, a man aged 60, was previously presented before the Manhattan Dermatological Society on Oct 14, 1947, with multiple lesions on the trunk and legs of about twenty years' duration

DISCUSSION

Dr Eugene F Traub This type of case is not uncommon, and one sees some who have taken arsenic and others who have not A relationship to psoriasis has also been observed, or, at least, patients have been seen in whom the multiple epitheliomas were perhaps mistaken for psoriasis, in others, psoriasis had been treated with arsenic and later multiple superficial epitheliomas developed In 1 case, the multiple epitheliomas had been mistaken for tinea and in a laboratory fungi were found in each of the lesions This in itself should have made any observer suspicious, because fungi are not found so readily in every lesion It is not known exactly how arsenic influences or brings about these lesions or just what the effect of sunlight may be A great deal has been said about treatment, and it has been said that the lesions are sometimes more difficult to cure than the ordinary basal cell lesion on the face This has not been my experience, as improvement occurs with desiccation and curettement, either with or without roentgen therapy, and sometimes a sufficiently large dose of roentgen rays clears up the early lesions also

Dr Joseph L Morse What is the consensus as to treatment?

Dr J Gardner Hopkins I believe that roentgen rays are effective in this type of basal cell epithelioma Atrophy does occur in the area, but it is not a particularly threatening type In desiccating lesions on the trunk one is apt to see secondary infections My inclination would be to treat these lesions with roentgen rays first and then use desiccation for recalcitrant areas

Dr Wilbert Sachs The patient has different types of lesions seborrheic dermatitis, lesions similar to Bowen's disease, superficial basal cell epitheliomas and arsenical keratoses on the palms The lesions on the lower extremities are basal cell epitheliomas, corroborated by the microscopic observations The quantity of radiation necessary to destroy lesions which have been present for twenty to thirty years is large, and such therapy is rather radical However, such lesions occasionally do become active and heroic methods are needed

Dr David Bloom I have had occasion to observe patients with psoriasis who took organic arsenic and had arsenical keratoses on the palms and soles and, in addition, basal cell epitheliomas on the trunk and squamous cell epitheliomas on the extremities I believe that in this case there is a causal relationship between the ingestion of arsenic and the development of epitheliomas

Dr Charles Wolf These cases illustrate the fact that disseminated epitheliomas are always caused by drugs or actinic exposure Fortunately, in these cases the history is straightforward One does encounter cases in which the patient denies taking arsenic, but it must be remembered that it may be ingested in an occult way, as through the food or occupation As to therapy, I feel that where there are so many lesions on the body it is inadvisable to give radium or roentgen

DR GERALD F MACHACEK In the sections one finds microscopic evidence of the formation of tubercles I am, however, not certain that from this evidence alone one should accept the diagnosis of tuberculosis cutis Not so long ago I saw a similar case, that of a young person suffering from exfoliative dermatitis for many years Microscopic examination of sections from his skin showed not dissimilar tuberculoid infiltrations, but I was able to show to my own satisfaction that they were foreign body reactions to epidermal inclusions Others have reported and I have seen "tubercles" in cutaneous lesions of leukemia

DR HOWARD FOX I may say that the patient has no evidence of tuberculosis as far as I can find out He is perfectly well and has no itching, the only peculiar fact is the surgical reaction which he had on two successive occasions after herniorraphy

Squamous Cell Epithelioma, Grade 3 Presented by DR JOHN C GRAHAM

Juvenile Acanthosis Nigricans Presented by DR FRED WISE

Vitiligo with an Elevated Border Presented by DR FRED WISE

A L, a boy aged 13, registered at the Skin and Cancer Unit on Feb 26, 1946, presenting depigmented patches of two months' duration A vitiliginous spot first appeared on the penis, about one to two weeks later a spot appeared on the forehead, two weeks later on the left eyebrow and a month later on the left side of the forehead at the hair margin

The patient presents depigmented white patches on the forehead, left side of the neck, left eyebrow, shoulder and penis They vary in size from 1 to 3 cm The depigmented spot on the left side of the forehead is round, of silver dollar size and encircled by an evenly, slightly raised, threadlike border In the middle of the forehead is a blackish, depigmented, half-dollar-sized, round spot, which has been present since birth, surrounded by a depigmented zone of 0 5 cm The results of the routine laboratory tests were normal

From a section taken from the depigmented patch with the raised border Dr Charles F Sims made the diagnosis of superficial exudative inflammatory process The description follows The epidermis is slightly irregular Its surface is covered in part by a very mild, loosely laminated horny layer At several points the granular layer has all but disappeared The basal margin is pigmented throughout one portion of the section and relatively nonpigmented in the remaining portion There are scattered chromatophores The rete pegs are somewhat irregular, and at some points of the basal layer liquefaction has taken place At the latter point there is a mild cellular reaction composed for the most part of small round cells The vessels of the upper part of the corium are moderately dilated and surrounded by a sparse cellular reaction composed for the most part of small round cells Numerous vacuoles apparently due to edema are present at several points in the corium

DISCUSSION

DR EUGENE F TRAUB A similar case was presented at the American Dermatologic Association, Inc, meeting in Chicago about two years ago I do not recall exactly how the peculiar border was explained, except that there may be some inflammatory process at work and with the peripheral extension of this inflammatory and slightly elevated border an area of depigmentation is

treatment for fear of sequelae which are irreversible, especially in the later decades of life Bone marrow activity is at a low ebb, and, therefore, administration of actinic rays is fraught with greater danger than when they are given to a younger skin I would therefore advise local excision as the better and safer procedure with so many lesions

DR JOSEPH L MORSE We all realize that arsenic has some relation to the production of basal cell epithelioma It is interesting that 2 such patients should be encountered at one meeting, one showing arsenical keratoses and the other not, but both with a history of ingestion of potassium arsenite solution, and it seems more than a coincidence that in both patients epitheliomas should have developed I have treated some of these lesions, and I think that they can be easily destroyed by electrodesiccation and curettage, certainly with better cosmetic results than this woman shows, and at the same time with no chance of radiation sequelae

Allergic Eczematous Cross Sensitization to Paraphenylendiamine and Several Azo-Dyes Certified for Use in Foods, Drugs and Cosmetics (Contamination of an Innocent Cosmetic with Paraphenylendiamine.)

Presented by DR RUDOLF L BAER and DR MORRIS LEIDER

S B, a woman aged 38, a worker in leather sundries, presented an eczematous eruption on the hands, arms, back and chest of eight months' duration Initial patch tests with a series of common eczematogenic allergens revealed a strongly positive (3 plus) reaction to paraphenylendiamine With this lead, additional tests were done, with the results noted in table 1

At this presentation the patient exhibits the results of patch tests applied forty-eight hours ago (table 2)

DISCUSSION

DR BEATRICE M KESTEN There is a crisscross sensitivity to adhesive tape I am not impressed by the cutaneous reaction to a test to nylon This woman wears nylon stockings, and she has no dermatitis on the legs I wonder whether she is so cross sensitive The results of patch tests as seen tonight do not exhibit it Perhaps she is sensitive to some of the ingredients in adhesive tape, and it might be well to test that possibility Instead of incriminating the numerous substances of which Dr Baer speaks, it might be that the patient is sensitive to paraphenylendiamine, a substance with which she comes in contact and to which she gives a positive reaction in patch tests

DR MARION B SULZBERGER If it can be shown that there are cases of cross sensitization between ordinary certified food dyes and other dyes commonly encountered in objects which come in contact with the skin from without, this might have a most important bearing on the difficulty of clearing up certain eczematous dermatoses when one has removed the offending external dye allergens Such refractoriness could perhaps be caused by relatives of the dyes being encountered in foods Moreover, it is possible that some eczematous or fixed eruptions which were reported as due to foods were really due to the dyes in these foods Because of the far reaching importance of these observations, I would again ask the presenter whether he considers the patch test reactions, as seen tonight, significant? I am inclined to agree with Dr Kesten that the patient tonight does not show any unequivocal reactions to nylon-dyes or other dyes

DR RUDOLF L BAER I agree with Dr Kesten and Dr Sulzberger that the test results in this patient are poor examples for demonstration I observed that several such "certified" azo dyes produced more strongly positive reactions in a

left Incidentally, this boy had a pigmented hairy nevus on the forehead, near the hair margin One of the patches of depigmentation involves this nevus, which is rapidly losing its pigment as a result.

DR A BENSON CANNON This is totally unlike any vitiligo that I have ever seen The linear rim around the white area is raised, red and firm, and the depigmented center is most likely the result of previous inflammation I think that we shall have to depend on the histologic examination for the diagnosis The raised lichenoid margin somewhat resembles lichen planus

DR FRED WISE It is interesting to call attention to the fact that a similar case was reported by Becker and Obermeyer (ARCH DERMAT & SYPH **36** 216 [July] 1937, and **37** 99 [Jan] 1938) Today the border is less elevated than when it was seen in the clinic, about two weeks ago Another interesting fact is that the patient has typical vitiligo of the penis and scattered vitiligo on other parts of the body, there are no signs of lichen planus and no signs of a border on the other lesions

A Case for Diagnosis (Poikiloderma? Localized Scleroderma?) Presented for DR GEORGE C ANDREWS by DR A BENSON CANNON

Neurodermatitis with Cataract and Asthma *Presented by* DR FRED WISE

F S, a young man aged 17, registered at the Skin and Cancer Unit on March 19, 1946, presenting lesions since infancy He has also been suffering with asthma since then The asthmatic attacks have been mild for the past several years The cataract in the left eye formed about three years ago He has five brothers and sisters who are well A cousin of his mother has asthma and had eczema The patient had chickenpox, German measles, scarlet fever, whooping cough and pneumonia in childhood and appendicitis at the age of 13 His general health has been good He complains of itching

The patient presents an almost perfectly symmetric and extensive eruption on the lower half of the forehead, face, front of the neck and upper and lower extremities On the face the lesions are distributed on the lower half of the cheeks, with the chin comparatively free On the upper extremities they commence just above the elbows, envelop the arms and end on the volar surfaces at the wrists, but include the dorsal surfaces, the hands and the terminal phalanx of the right middle finger The lesions are most pronounced on the lower extremities and encircle almost completely and uninterruptedly, except for the inner and upper surfaces of the thighs, the thighs and legs down to the distal half of the dorsal surfaces of the feet, terminating in a sharp margin They consist of heavily crusted oozing vesicular fissured patches, infiltrated and thickened to several millimeters The soles are hyperkeratotic, particularly the heels and the anterior metatarsal arches The back is uninvolved except for isolated spots On the chest, elbows and arms are fairly numerous pinpoint-sized to pinhead-sized, irregular, dry crusted patches on the back of the scalp In the groins the lymph nodes are enlarged to the size of goose eggs and in the axillas to cherry size

NOTE —The patient is hospitalized at the New York Post-Graduate Hospital Laboratory reports will be given later

DISCUSSION

DR GEORGE M MACKEE It is important, for medicolegal reasons, to know that spontaneous cataracts occur in this disease, otherwise roentgen treatment is likely to be unjustly blamed, as has not infrequently happened

number of patients with paraphenylendiamine hypersensitivity than in a series of "normal" control subjects Some of these dyes have primary irritant properties on human skin

There are many azo dyes that are certified by the Food and Drug Administration for use in food, drugs and cosmetics and others which are certified for use only in drugs and cosmetics Those azo dyes which were tested in this patient are certified for all three uses Their use is widespread, they can be encountered in such diverse products as nail polish, sausage casings, raspberry syrup and other beverages

We do not know yet what is the clinical importance of these reactions It is possible that these cross sensitizations to azo dyes may account for some of the chronicity in cases of dermatitis due to paraphenylendiamine, and perhaps also for

TABLE 1 —*Results of Tests*

Test Substance	Reading	Source of Contact
Black suede leather	1 2 plus	Occupational
Rubber glove	3 plus	Therapeutic
Black satin dress	3 plus	Wardrobe
Brown dress A	1 2 plus	Wardrobe
Brown dress B	2 plus	Wardrobe
Navy blue dress	2 plus	Wardrobe
"Fresh" deodorant (old jar)	2 plus	Cosmetic
"Fresh" deodorant (new jar)	Negative	Cosmetic

TABLE 2 —*Results of Additional Tests*

Test Substance	Reading	Potential Source
Paraphenylendiamine	4 plus	Fur dyes, hair dyes, etc
Red No 1 *	Negative	Foods, drugs, cosmetics
Red No 2 *	Negative	Foods, drugs, cosmetics
Red No 3 *	Negative	Foods, drugs, cosmetics
Fed No 4 *	Negative	Foods, drugs, cosmetics
Red No 32 *	Negative	Foods, drugs, cosmetics
Yellow No 3 *	2 plus	Foods, drugs, cosmetics
Yellow No 4 *	2 plus	Foods, drugs, cosmetics
Yellow No 5 *	Negative	Foods, drugs, cosmetics
Yellow No 6 *	Negative	Foods, drugs, cosmetics
Orange No 1 *	Negative	Foods, drugs, cosmetics
Orange No 2 *	Negative	Foods, drugs, cosmetics
Nylon stocking	2 plus	Wardrobe

* Food drug and cosmetic dyes

some of the unexplainable flare-ups This particular patient showed a very mild reaction to tests with the dyed nylon stockings In most cases of paraphenylendiamine hypersensitivity, reactions to nylon stockings containing these azo dyes are much stronger However, the fact that the patient gives a positive reaction in a patch test but does not have a stocking dermatitis is not surprising, because even in cases of dermatitis due to dyes in nylon stockings, with strongly positive reactions, the entire leg is usually not involved In most cases only the dorsa of the feet and the popliteal spaces are involved, showing that the eruption tends to develop in sites where maximal extraction is likely to occur

As far as the deodorant cream is concerned, it is possible that the patient contaminated it with the nail polish, which may contain one of the azo dyes

DR EUGENE F TRAUB Why was the deodorant considered to be contaminated by nail polish rather than by paraphenylendiamine?

DR MAURICE J COSTELLO I had a patient who had received a great deal of roentgen rays (from another physician) to the face, and even though the eyes were covered with lead protectors bilateral cataracts developed The ophthalmologist attributed the cataracts to the roentgen ray therapy until he was informed of the association of juvenile cataracts with neurodermatitis He had never heard of spontaneous cataracts forming in young persons with the dermatosis and had always thought that they were caused by roentgen rays This is of medicolegal importance

George C Andrews, M D, *President*
George M Lewis, M D, *Secretary*
April 23, 1946

Sycosis Vulgaris Presented by DR HOWARD FOX

C V W, aged 38, a guard by occupation, was discharged from the Army five years ago, after three years of service During the last fourteen months in the Army he was constantly receiving treatment in various hospitals He now presents an eruption confined to the upper lip and entire bearded area, which was previously of pustular type and now resembles a scaling eczema

Treatment in Army hospitals consisted chiefly of penicillin, roentgen rays and ultraviolet irradiation He received an enormous amount of penicillin, administered both by intramuscular injections and as an ointment He received a total of three hundred and fifty injections, in three courses of treatment, which completely failed to influence the eruption He also had seven fractional doses of roentgen rays (without causing epilation) at the Walter Reed Hospital, after which he was practically well for two months The disease then recurred in the same severe form He was at one time given general and local ultraviolet radiation for six weeks, which was followed by a deep tan on the body, but had no effect on the eruption On another occasion, he used quinolor® ointment (contains 10 per cent benzoyl peroxide and 0 5 per cent quinolor® [a mixture of three chlorine derivatives of 8-hydroxyquinoline] in a base of equal parts of petrolatum and wool fat) in various strengths for two weeks with slight benefit The patient appears to be in good general health and is again working full time He was first seen by me on April 1, 1946, and since then he has used quinolor® ointment once a day with slight improvement

DISCUSSION

DR ANTHONY C CIPOLLARO Cases of sycosis vulgaris tax the resourcefulness of the dermatologist I find that manual epilation of infected hairs is effective Tyrothricin, penicillin and other new antiseptics in easily absorbable bases, combined with injections of toxoid and small weekly doses of roentgen rays improve or keep under control most cases of sycosis vulgaris I certainly oppose the use of roentgen rays for the purpose of producing permanent epilation

DR PAUL E BECHET I believe that the local use of penicillin in sycosis vulgaris should be discontinued if no improvement occurs after it has been applied for a week, as cutaneous reactions from penicillin are, in my experience, greatly increasing in number—so much so as to become almost commonplace I have

DR RUDOLF L BAER It is possible that some of the occupational materials had contaminated the old jar of deodorant cream However, it is conceivable that certified azo dyes contained in the nail polish might have been responsible

Lupus Vulgaris (Treated with Calciferol). Presented by DR MARION B SULZBERGER

A S, a woman aged 33, was previously presented at the New York Dermatological Society, on Oct 24, 1939 She is shown tonight to illustrate the good results of calciferol (crystalline vitamin D_2) therapy and the simpler dosage schedule employed

In 1924 the patient first noted an eruption on the right cheek consisting of small erythematous and tumid nodules which healed with central whitish depressed scars The eruption gradually spread to involve the entire right cheek, chin, nose, forehead and both lips Previous treatment included radium, roentgen rays, electrodesiccation, tuberculin, Kromayer lamp, generalized ultraviolet irradiation and gold sodium thiosulfate, given by various dermatologists and clinics, with no great improvement

On May 3, 1946, vitamins A and D_2 (100,000 units of each daily) were given, in addition to tuberculin and ultraviolet irradiation On October 4, all other treatment was discontinued and the patient was given ertron® (concentrated vitamin D preparation) capsules daily (50,000 units) plus calcium lactate (4 0 Gm daily) Since that time she has shown gradual, consistent and finally great improvement No new nodules have appeared, and there has been no peripheral spread The skin has become less erythematous and has assumed a more normal color In addition, it has been more flexible, and the patient stated that there is increased mobility of the circumoral tissues especially, which previously interfered with mastication and speaking

Lupus Vulgaris, Improved with Calciferol Therapy Presented by DR JACK WOLF

V T, a man aged 47, is presented from the New York Skin and Cancer Unit with an eruption in the left postauricular region of approximately fifteen years' duration He was born in Italy and has lived in the United States for the past twenty years The eruption has never been troublesome, and the patient presented himself only recently because of the gradual extension of the process

He presents an erythematous, well marginated, brownish red patch involving the posterior auricular region and extending on to the temporal and mastoid regions The lobe of the ear is involved, and well developed small nodules are present in this location The process has improved greatly since calciferol therapy was instituted about four weeks ago, the nodular lesions have regressed considerably

The Wassermann reaction of the blood was negative, and the urine revealed no abnormalities There was no reaction to the intradermal tests with tuberculin in dilutions of 1 100,000 and 1 10,000

A histologic report by Dr A Hyman stated that in the upper part of the cutis there were groups of epithelioid and giant cells in tubercle arrangement There was a banal infiltrate around the tubercles

DISCUSSION

DR MAURICE J COSTELLO Calciferol is a good medicament for lupus vulgaris I have also treated patients with generalized lichenoid sarcoid with calciferol with equally good results and think that it is worth a trial in this dermatosis also

observed two types of reaction caused by penicillin in sycosis, some patients showing a great increase in pustules and inflammation after its local use for a few days and others an acute vesicular outbreak with much redness and discomfort within forty-eight hours after its first application

I have used quinolor® in sycosis plus roentgenotherapy, 75 r once a week, with such satisfactory results that this method is used by me almost exclusively

DR MAURICE J COSTELLO I think that the best treatment for these cases is compound quinolor® ointment, and, if properly rubbed in three times daily, before and after shaving and at night, it is effective

DR JOHN C GRAHAM I have had poor results with penicillin in the treatment of sycosis vulgaris I have had better results with compound quinolor® ointment, but have had few permanent cures

DR FRED WISE I share the views of those who favor manual epilation, it is one of the most important methods of therapy The patient should be taught not to pull the skin out with the hair and to allow his beard to grow for two or three days I feel that some of these cases are almost incurable A fluid preparation known as intraderm® (antifungal agent) combined with tyrothricin is of considerable value in the treatment of this disease

DR EUGENE F TRAUB This patient has had much treatment, but the best remedy for so severe a condition has not as yet been used, and I see no reason why a careful roentgen epilation should not be done It has been my practice to do this in the bearded area, using a divided dose and alternating with ultraviolet rays from a cold quartz lamp to control and prevent a pustular flare-up This has always been successful, and the patient is free of eruption in approximately six weeks from the date of the first treatment I believe that the aftercare from this point on is also extremely important because there is a tendency to relapse Therefore, while the new hair is growing back, I usually have the patient use either quinolor® ointment, ammoniated mercury or some other similar mildly antiseptic cream If the new hair is kept free of infection, the patient is permanently cured

DR A BENSON CANNON Any case of folliculitis is difficult to cure While manual epilation is the method of choice in treating localized areas, in cases with generalized sycosis, it is almost impossible and certainly impractical to pull out all the hairs About a year ago I presented a patient with generalized sycosis of several years' duration who was cured with wet dressings and injections of penicillin and frequent potassium permanganate baths I had 3 cases of generalized sycosis cured with this treatment within three to six months

DR GEORGE M LEWIS In order to obtain maximum results from penicillin applied locally, some individualization in the strength of the application is desirable Cormia has found tests of sensitivity to the bacteria found in culture to be helpful in gaging the concentration of the penicillin to be used Empirically, one may use higher percentages of penicillin when the response is poor to standard strengths

DR GEORGE C ANDREWS I was impressed by the apparently infected lower teeth All the upper teeth have been pulled out The patient never had roentgenograms taken of his lower teeth His gums are retracted and show definite gingivitis, and I suspect that he has root abscesses I agree with those who prefer manual epilation and quinolor® ointment If sulfonamide drugs were not

DR FRANCIS PASCHER We now have 9 or 10 patients at the Skin and Cancer Unit who have been treated with calciferol for lupus vulgaris for approximately six months to one year About 75 to 80 per cent improvement is attained in about six to eight months of treatment, and then progress is much slower, or seems to come to a standstill The problem of how to treat the residua presents itself

DR ANTHONY C CIPOLLARO Calciferol certainly is not a cure-all for cutaneous tuberculosis, but it is the best remedy that dermatologists have ever had to combat this disease, as well as lupus erythematosus and other tuberculodermas It is also interesting to note that calciferol is derived from irradiated vegetable ergosterol and so is related to ultraviolet irradiation Up to the present the only effective treatment for lupus vulgaris has been ultraviolet irradiation, especially as carried out at the Finsen Institute at Copenhagen Now there is a remedy derived through the action of ultraviolet irradiation on ergosterol

DR RUDOLF L BAER In connection with the superficial nodules remaining after treatment with calciferol, Lomholt has recently advised a combination of calciferol and Finsen treatment Apparently the deep nodules cannot be reached by the Finsen treatment, and the superficial ones cannot be reached by calciferol He believes that the combined treatment may solve the problem

DR CHARLES WOLF One must always be on the lookout for atheromas of the capillaries of the kidney especially, and also of the smaller vessels of the myocardium Patients given calciferol and calcium should have frequent determinations of the blood calcium Where there are residua, an ointment containing 3 per cent calciferol is effective

DR MARION B SULZBERGER The answers to most of the questions asked are to be found in the recent literature At the New York Skin and Cancer Unit we used dosage schedules of 600,000 units, three times for the first week, twice for the second, third and fourth weeks and once weekly thereafter because we think it essential to work along the exact lines a predecessor has followed, to repeat as accurately as possible what was done originally, in order to see whether we obtain the same results as the original observer So we went to great pains to use the same doses and preparations as Charpy, getting the solutions of sterogyle 15® (vitamin D preparation) from France and treating our patients in the same way as was done there Then, having fully confirmed what earlier observers have said, we then used other preparations of vitamin D_2 and used modified dosage schedules I would hazard a guess that the optimum dosage might be different in each case, as with gold compounds and the arsenicals I think that the future and fundamental study of this form of treatment is important We know that this vitamin schedule is effective in some cases of sarcoidosis Is that an added argument in favor of the thesis that sarcoid is some form of tuberculous infection, or is vitamin D_2 (calciferol) also good for other types of granulomas not due to tubercle bacilli? If so, it might be good for tuberculoid leprosy, and many other important granulomatous infections At my suggestion, Dr Wade is planning to try it out in the tuberculoid and lepromatous forms of leprosy Will vitamin D_2 be valuable in treatment of any types of tuberculosis of the viscera, and if so, which forms? These and many other questions can be answered only when many investigators take up and extend this new form of treatment introduced by European dermatologists

Chronic Benign Familial Dermatosis (Hailey-Hailey) Presented by DR NATHAN SOBEL

R M, a man aged 72, is presented from the New York Skin and Cancer Unit with a rash which has been present intermittently for six years It started on the left side of the neck and now involves the dorsum of the chest, sides of the neck

used and sensitivity of the Staphylococcus to penicillin has not been tested, I would advise that this be done

DR HOWARD FOX I am grateful for this discussion I shall see that the man has a roentgenogram of his lower teeth in a search for abscesses He has certainly had penicillin to the limit From what I have read, I have come to the conclusion that penicillin is often a poor remedy for sycosis vulgaris As to fractional doses of roentgen rays, I have had poor results I think that quinolor® ointment is the best remedy, though it may have to be continued for months As Dr Cannon said, it is not feasible in cases of profuse eruption to pull out all the hairs I shall advise the patient to rub in the quinolor® ointment vigorously three times a day

Lymphogranulomatosis Benigna (Schaumann's Disease) Presented by DR FRED WISE

A A, a Negro woman aged 35, registered at the Skin and Cancer Unit April 4, 1946, presenting lesions of four months' duration The patient had smallpox at 8, therapeutic abortion at 16 and supravaginal hysterectomy at 28 years She complains of weakness, cough, anorexia, constipation and nocturia During the past eight months she lost 33 pounds (15 Kg) in weight

On both parotid areas are symmetric hen's egg-sized fixed swellings Axillary and epitrochlear lymph nodes are enlarged The liver is enlarged to 3 finger-breadths below the costal margin The spleen is palpable and hypertrophied

Examination showed a pea-sized, raised, painless, nontender nodule on the upper lip and one on the chin, ten similar nodules are located on the small of the back and scattered isolated growths on the trunks and extremities Herpes zoster, in the form of a vesicular erythematous eruption, extends along the entire left sixth rib

The hemogram was normal Routine examination of the chemical content of the blood revealed 8 5 mg of urea nitrogen (normal 25 to 35), 21 mg of nonprotein nitrogen in one hundred cubic centimeters of whole blood (normal 160 to 230), 230 mg of cholesterol in one hundred cubic centimeters of plasma The icteric index was 7 1 The cephalin-cholesterol flocculation test gave a plus-minus result

Roentgenograms of the long bones showed small cystlike areas at the heads of several phalanges of both hands Examination of the eye revealed an enlargement of the peripheral portion of both lacrimal glands The orbital portion on the left side had a shotty feel On retracting the lower eyelid several match-head-sized nodules are exposed and hyaline-like excrescences at the upper borders of the tarsi of both lids are present There is no uveitis or iridocyclitis

The patient has chronic atrophic nasopharyngitis with suspicious small nodules on the uvula and a nodule on the laryngeal surface of the epiglottis and on the anterior commissure of the subglottis

The histologic section from one of the lesions showed Boeck's sarcoid Dr Charles F Sims interpreted the observations as follows The epidermis is somewhat flattened Throughout the upper middle part of the cutis and extending downward into the deep part of the corium are numerous well defined cellular masses composed of epithelioid and giant cells These masses do not appear to be undergoing necrosis There is little small round cell infiltration

Hodgkin's or lymphoblastoma type and the type described by Lewis, which seemed to be on an allergic basis and simulated changes seen in periarteritis nodosa In the case of eosinophilic granuloma of the bone reported by Curtis there were elevated granulomatous cutaneous lesions I saw a patient today with ulcerative lesions with decided changes in the bones of the skull which makes the disease in this case similar to Hand-Schuller-Christian's disease and Letterer-Siwe's disease My co-workers and I have observed a patient with multiple small granulomatous lesions with similar cystic lesions and rarefaction in the bones In another case in which our original diagnosis was histiocytoma, there were multiple small nodular lesions in the skin resembling xanthoma and bony lesions subsequently developed in the mandible Farber of Boston groups eosinophilic granuloma of the skin, Letterer-Siwe's disease and Hand-Schuller-Christian's disease together as variants of the same process and regards any evidence of deposition of fat in the tissue as a secondary degenerative phenomenon He therefore would differentiate these conditions from xanthomatosis and diseases of lipid metabolism Some years ago, however, Weidman reported a case of xanthoma disseminatum in association with Hand-Schuller-Christian's disease, and there are other such cases in the literature so that the exact classification of eosinophilic granuloma of the bone and skin remains to be determined

Noduloulcerative Syphilid of the Chest Wall Presented by Dr Herbert Rattner and (by invitation) Dr H Rodin and Dr N L Baker

Ulceronodular Syphilis of the Abdomen Presented by Dr James R Webster and (by invitation) Dr J Graffin

A Case for Diagnosis (Pyoderma Faciale?) Presented by Dr Theodore Cornbleet and (by invitation) Dr D Cohen and Dr J Graffin

Bromoderma, Granulomatous and Acneform Presented by Dr David V Omens and (by invitation) Dr Harold D Omens and Dr J Graffin

A Case for Diagnosis (Blastomycosis? Bromoderma?) Presented by Dr Francis E Senear and staff

Lymphangiectasis of the Vulva Presented by Dr Herbert Rattner and (by invitation) Dr H Rodin and Dr N L Baker

A Case for Diagnosis (Lichen Striatus? Nevus?) Presented by Dr Theodore Cornbleet

A Case for Diagnosis (Meleney's Ulcers or Pyoderma Gangrenosum?) Presented by Dr Theodore Cornbleet and (by invitation) Dr H Shorr and Dr N L Baker

Squamous Cell Epithelioma at the Site of Old Lupus Vulgaris Which Had Been Treated with Roentgen Rays Presented by Dr Theodore Cornbleet and (by invitation) Dr David Cohen

Pityriasis Lichenoides of Juliusberg Presented by Dr E A Oliver

Parapsoriasis Guttata (Pityriasis Lichenoides Chronica) Presented by DR STEPHEN ROTHMAN and (by invitation) DR Z FELSHER and DR R SNAPP

Pityriasis Lichenoides Chronic Varioliformis Presented (by invitation) by DR MAURICE OPPENHEIM and DR W A YACULLO

Pityriasis Lichenoides et Varioliformis Acuta Presented by DR EDWARD A OLIVER and (by invitation) DR A B HENNINGSEN

Lupus Miliaris Disseminatus Faciei Presented by DR EDWARD A OLIVER and (by invitation) DR H F GARRARD

Sarcoidosis, Cutaneous Lesions of Boeck and Darier-Roussy Type Presented by DR FRANCIS E SENEAR and staff

A Case for Diagnosis (Acrodermatitis Atrophicans Chronica?). Presented by DR FRANCIS E SENEAR and staff

A Case for Diagnosis (Keratosis Pilaris?) Presented by DR M H EBERT and (by invitation) DR VERA LEAF

Pustular Psoriasis Presented by DR M R CARO, DR STEPHEN ROTHMAN and (by invitation) DR R SNAPP

Cicatrizing Alopecia Presented by DR DAVID V OMENS and (by invitation) DR HAROLD D OMENS

Leukemia Cutis Presented by DR FRANCIS E SENEAR

Francis W Lynch, M D, *President*

Leonard F Weber, M D, *Secretary*

May 21, 1947

A Case for Diagnosis (Erythrasma?). Presented by DR T CORNBLEET and (by invitation) DR H SCHORR and DR J GRAFFIN

Granuloma Inguinale Treated with Streptomycin Presented by DR M H EBERT and (by invitation) DR N BAKER

O N, a Negro aged 46, has been ill for fifteen years He has been a bed patient in the Cook County Hospital for the past twenty-eight months He was admitted in January 1945 with extensive ulceration of the inguinal areas, scrotum and perineum Smears of these areas showed Donovan bodies From July 1946 to February 1947 he was treated with podophyllum solution (20 per cent in liquid petrolatum) with some improvement On April 18 treatment with streptomycin was begun and given for one month, 120,000 units every three hours The process on the inguinal areas and scrotum has healed, on the perineum there is still a small ulcer (3 by 5 cm)

DISCUSSION

DR HENRY E MICHELSON (by Invitation) I was glad to have the opportunity of seeing this patient I agree with the diagnosis of Schaumann's disease, and I think that some common term should be used for all of these sarcoid conditions, like sarcoidosis I think that this disease is a general condition, not necessarily a system disease, for the various systems most commonly involved are the lymph nodes, skin, lungs and bones However, even the meninges may be involved There is still much studying to be done on the subject It is strange that the Scandinavians see so much in their country and here the disease is seen so commonly in Negroes I feel that one should take a broad view of this disease, have an open mind as to causation and not expect the histologic picture to be as precise as has been believed in the past The course of sarcoidosis is variable some patients having complete remissions and some having the disease for many years

DR. MAURICE J COSTELLO I think that the herpes zoster in this case is an interesting feature and that it is due to pressure on the posterior nerve roots by the lesion of this disease A similar mechanism occurs in Hodgkin's disease

DR. ANTHONY C CIPOLLARO It is my understanding that in a number of these cases pulmonary and even miliary tuberculosis develops later

DR FRED WISE I am grateful for this discussion, from which I have gained considerable knowledge The only point against the established diagnosis of Schaumann's disease is the absence of uveitis perhaps the process is not sufficiently advanced to have caused this symptom I have in mind fever therapy for this patient

A Case for Diagnosis (Annular Atrophic Lichen Planus? Scleroderma?). Presented by DR FRED WISE

Epidermolysis Bullosa, Spina Bifida Occulta, Vitamin Deficiency Associated with Ichthyosis Presented by DR A BENSON CANNON

A Case for Diagnosis (Sarcoid? Granuloma Annulare?) Presented by DR. FRED WISE

Epidermolysis Bullosa Confined to the Palms and Soles Presented by DR MAURICE J COSTELLO

L C, a girl aged 19, has had recurring large thick-walled painful bullae on the bearing surface of the feet and on the palms since she was 3 years of age The eruption on the soles is present mainly in the spring and summer, when she is more inclined to walk Blisters occur on the palms at points of pressure after such household duties as ironing clothes In addition, she presents a number of calluses on the pressure points of the dorsal aspect of the toes There is some redness and scaling of the dorsal aspect of the last phalanx of the fingers The feet have an aged appearance Yesterday it was observed that, in addition, the patient complains of chapping, redness and scaling of the lower third, anterior surface of the legs and the tip of the nose in cold and windy weather Treatment has been palliative, consisting of rupturing the vesicle and use of potassium permanganate foot baths

A Case for Diagnosis (Lichen Planus Pilaris? Parapsoriasis? Premycotic Stage of Mycosis Fungoides?) Presented by DR MAURICE J COSTELLO

Eosinophilic Granuloma of Pituitary Gland, Lungs, Bones of the Skull, and Skin Presented by DR GEORGE M LEWIS

M T, a woman aged 33, is presented from New York Hospital She was well until ten years ago, at which time she had severe polydipsia, polyuria, amenorrhea and loss of libido, clinically typical of diabetes insipidus Roentgen studies disclosed a normal sella turcica, but there were multiple rounded areas of destruction in the occipital and parietal bones, compatible with the diagnosis of eosinophilic granuloma of bone Similar lesions were demonstrated in the frontal region three years later At this time a necrotic area was found in the mandible, and on section it was found to be typical of eosinophilic granuloma of bone with "fairly dense connective tissue which was diffusely infiltrated by myelocytes of various forms and a great number of eosinophils" Four years after first observation, roentgen therapy, in a dosage of 400 r, was given to the osseous lesions of the skull and resulted in their complete involution There was no improvement in the diabetes insipidus following roentgen therapy, and symptoms, partially controlled by pitressin® (a preparation of the pressor principle of the posterior lobe of the hypophysis), have persisted to date

Granulomatous vulvar lesions were first noted four years after the onset of the disease These have gradually become more pronounced and extensive to date, six years later Eighteen months ago burning and redness were noted in the axillas and have been followed by the gradual development of granulomatous lesions similar to those on the vulva During the past four months low grade paronychial lesions and gradual destructive changes in the finger nails and toe nails have occurred

The axillas, vulvar region, perineum and adjacent aspects of the thighs are the seat of an extensive, moist, hypertrophic and vegetating granulomatous process The paronychial tissues are reddened and exude purulent material The nail substance has largely disappeared Chronic gingival lesions, now cleared, have resulted in the gradual loss of all the teeth

Repeated blood cell counts have revealed slight secondary anemia and inconstant, moderate leukocytosis Eosinophilia has never been detected Sternal marrow study was within normal limits Results of serologic tests of the blood were negative on several occasions Total protein was 8 Gm, the albumin-globulin ratio was 4 9 to 3 1, cholesterol values were normal Cultures from the granulomatous lesions have revealed hemolytic Staphylococcus aureus and Staphylococcus albus, nonhemolytic streptococci and a gram-negative bacillus resembling Bacillus Ducreyi Results of examination of curetted tissue for Donovan bodies were negative The reaction to the Frei test was negative Routine roentgen examination of the chest eight months ago showed a diffuse generalized eosinophilic infiltration in both lungs Results of examinations of the stool for ova and parasites have been negative on two occasions

A section taken from granulomatous lesions showed numerous large mononuclear cells, plasma cells and eosinophils, the latter occurring both perivascularly and diffusely through the section Moreover, eosinophilic granules were noted lying free in the tissue The blood vessels were the seat of extensive endarteritis

While the eosinophilic granulomas of bone disappeared after roentgen therapy, there has been no improvement in the diabetes insipidus to date The patient has

DISCUSSION

DR GLORGE C ANDREWS I have as patients a brother and sister who have this disease limited to the palms and soles They have atrophy of the phalanges and the skin of the hands and feet The brother has some other lesions on his body but the sister has lesions only on her palms and soles My patients have atrophy and bullae, and atrophy of the digits, and present definite epidermolysis bullosa of fifteen years' duration This patient to my mind has hyperkeratosis and bullae I am not sure whether she has epidermolysis bullosa I presented a similar case before the New York Dermatological Society on Jan 23, 1945

DR J GARDNER HOPKINS This case reminds me of one reported in the November issue of THE ARCHIVES, also under the same diagnosis, with the disease limited to the palms and soles, but with no other signs of epidermolysis bullosa, and I wonder whether it was really that disease

DR HOWARD FOX I agree with Dr Hopkins I have received a number of articles from men in the Army or Navy describing cases with the condition limited mostly to the soles These men have eventually had to be discharged from the service They were often considered to be suffering from dermatophytosis at the outset, but eventually the correct diagnosis was made

DR MAURICE J COSTELLO This patient presents lesions almost at will After ironing clothes for a time large bullae develop on her palm, and always after walking three or four blocks bullae develop on her soles I have seen quarter-sized and half-dollar-sized, thick-walled bullae on her palms and soles

Widespread Papulosquamous Eruption, Neurosyphilis Presented by DR A BENSON CANNON

V V, a 42 year old Puerto Rican woman, was admitted to City Hospital for a generalized rash of three months' duration She had been in good health until three months prior to admission, when she suddenly began to experience severe frontal headaches, fever, malaise and anorexia At the same time there appeared a rash on the flexor surfaces of the arms and forearms The rash spread rapidly and became generalized The patient did not receive any therapy She was admitted to the hospital on April 15, 1946, having been referred from the Vanderbilt Clinic

The patient has been a widow for three years She has five children, all in good health The oldest is 25 years of age and the youngest 9 years One miscarriage occurred seven years ago

Physical examination discloses a well nourished Puerto Rican woman There is a generalized papulosquamous eruption involving the entire cutaneous surface, including the palms, feet and face Lesions are symmetric and superficial They are brownish red and covered with adherent scales The lesions resemble psoriasis The mucous membranes are not involved There are no lesions in the throat There are no lesions in the genital or anal regions The pupils react in accommodation but not to light The knee jerk is exaggerated, the ankle jerk is present The Romberg reaction is negative

The Ducrey and Frei reactions were negative Examination of the spinal fluid showed 12 cells, 0 01 per cent protein, colloidal gold 4444321000 Results of dark field examination of material from the lesions were negative on April 16 The Kline reaction of the blood was 4 plus on April 12 The Wassermann

gained 25 pounds (11 Kg) in the past ten years The cutaneous lesions have shown gradual improvement following various types of local therapy and the administration of roentgen rays

DISCUSSION

DR GERALD F MACHACEK I do not wish to take issue with the diagnosis, but there are indications here of what might be called multiple myeloma From a section of the skin, and taking into consideration that the blood cell count was within normal limits, I think that the changes suggest aleukemic leukemia, from the many monocytic cells within the vascular lumens

DR MAURICE J COSTELLO I think that Dr Lewis, about three years ago, presented a case of eosinophilic granuloma confined entirely to the skin, with a large tumor mass on the back

DR GEORGE M LEWIS This case is almost unique in that there is authenticated involvement of bones, lungs and skin It is interesting that roentgen therapy is rapidly successful in curing the bone disease and apparently in curing the lung disease Roentgen therapy has also helped the cutaneous lesions in this patient The essential histologic changes appear in the blood vessels, which at first show swollen endothelial cells with progressive endarteritis with narrowing of the lumen The infiltrate at first is focal but later diffuse through the tissues The infiltrate also changes from a polymorphous type to one predominantly eosinophilic

Solid Edema of the Face and Neck Occurring in the Course of Infectious Eczematoid Dermatitis Presented by DR MAURICE J COSTELLO

Eugene F Traub, M D, *President*
George M Lewis, M D, *Secretary*
Jan 28, 1947

A Case for Diagnosis (Melanoma?) Presented by DR PAUL E BECHET

V P, a woman aged 53, stated that sixteen years ago she noticed a small tumor on her right cheek which increased considerably in size within a year It was removed but in what manner she does not remember Two years later it recurred, and in the past thirteen years no attempt has been made to treat it In the past year the patient states that the lesion has increased in extent On inspection, she presents a dark red patch about 50 mm in diameter, with a distinct, elevated and indurated border and in its upper part a black, sharply outlined, somewhat raised, rounded area about 30 mm in diameter The patient states that the melanotic features have been present for six years Her health is good, and there is no evidence of metastasis anywhere There are no similar lesions elsewhere on her body

DISCUSSION

DR JOHN C GRAHAM I would have a plastic surgeon remove the lesion, which is commencing to show malignant changes It is undoubtedly melanotic, and I think it should be widely removed and a graft set in

DR MAURICE J COSTELLO As the lesion has been present for sixteen years, I would be inclined to do nothing radical It may last another sixteen years

reactions of the blood and the spinal fluid were both 4 plus on April 16 The patient has received 4,000,000 units of penicillin, 100,000 units every three hours

DISCUSSION

DR RAY H RULISON It is rather curious that, in a person obviously with neurosyphilis and with Argyle Robertson pupils, there should be such an extensive syphilitic eruption as this Cutaneous eruptions are relatively rare in neurosyphilis How would this eruption be classified, assuming it to be a syphilitic eruption?

DR A BENSON CANNON One frequently sees involvement of the nervous system in cases of early syphilis and especially in the late secondary stage This patient's cutaneous lesions have greatly improved with penicillin

NOTE—The diagnosis from biopsy of the cutaneous lesion was syphilis All lesions disappeared after the penicillin injections

Acanthosis Nigricans Presented by DR FRED WISE

A S, a boy aged 12, registered at the Skin and Cancer Unit on April 16, 1946, presenting cutaneous lesions of eight months' duration He has two brothers, aged 5½ and 3½ years, who do not have any cutaneous disease He had measles, chickenpox, scarlet fever, German measles and mumps during childhood and a streptococcic infection of the throat and recurrent infections of the left ear His appendix was removed at the age of 10 He was also subject to mild attacks of hay fever His maternal grandmother died at the age of 56 from a tumor of the kidney which became polycystic The paternal grandmother had a kidney removed "for some ailment," and two years later the other kidney became affected and she died at 52 The paternal uncle died at 35 after a kidney removal Both grandfathers died of "heart attacks" Obesity is a familial trait Most of the members of the family from the grandparents down have been and are obese

The mother stated that the child's neck was always darker than the rest of the body, and this was thought to be due to exposure to the sun The boy is of average intelligence He feels strong and well, except for occasional attacks of frontal headaches

A "sore" area first developed on the right side of the neck, this would clear up for a week or two and then recur after he wore rayon shirts or used soap When he avoided rayon shirts and soaps the soreness would regress, leaving rough areas which would become rougher after each attack of soreness Two months later the patches began to spread around the neck The pigmentation in the axillas appeared at the same time as those on the neck The patch on the left cubital region developed about two months ago

Examination shows blackish pigmentation on the neck, axillas and left cubital region The neck shows black dry nontender somewhat infiltrated patches which are irregular in outline, ill defined and intermingled with depigmented patches They feel rough, like sand paper The pigmented areas blend gradually into the surrounding integument There are similar symmetric patches in both axillas, blackish brown, and well defined, silver dollar-sized, dull brownish patch in the

I have had at least half a dozen patients in my practice for whom the diagnosis of malignant melanoma was made and confirmed by histologic study who have done well One has survived six years, a second nine years and a third ten years

DR GEORGE C ANDREWS I have seen superficial lesions of this character which continue for a long time However, I believe that the histologic diagnosis would be melanoma

DR. GEORGE M LEWIS If melanoma is seriously considered here, transillumination is a valuable method to demonstrate the extent of the lesion It is my impression that the lesion is a pigmented basal cell epithelioma or possibly a pigmented nevus and not a melanoma

DR PAUL E BECHET I greatly appreciate the discussion because of the involved therapeutic problem The fact that the lesion has been continuously present for thirteen years, with increase in size only in the past year, does in my opinion prove the presence of a low grade or transitional type of malignant process The patient denies the existence of any lesion on her cheek prior to the present one, so that it apparently occurred d'emblée sixteen years ago The opinions expressed in the discussion are somewhat divided as to whether or not one should intervene I shall take them carefully under consideration before making a decision, but my impression is that we are dealing with a malignant lesion which, though present for sixteen years with no apparent metastasis or much increase in size, remains potentially dangerous and that it would be better to excise it widely and subject the tissue to microscopic examination than to leave it severely alone, with possible fatal results in the future

Necrobiosis Lipoidica (Without Diabetes) Presented by DR GEORGE M LEWIS

Leukoplakia of Buccal Mucosa (Excellent Result from Treatment with Electrodesiccation) Presented by DR A BENSON CANNON

Tuberculoid Leprosy. Presented by DR. MAURICE J COSTELLO

E P, a boy aged 5, from Willard Parker Hospital, was born in Puerto Rico His father died of pulmonary disease, and his mother is in a leprosarium in Puerto Rico She has had the disease at least seven years The boy was brought to New York by plane via Miami on June 23, 1946 He had about a dozen somewhat hyperpigmented, sharply circumscribed, dime to quarter-sized lesions with a thin, raised border These lesions are anesthetic to cold, heat, touch and the prick of a pin The ulnar nerves are enlarged, and the greater auricular nerve can be palpated

The Wassermann reaction of the blood was negative, as were the reactions to the Kline diagnostic and Kline exclusion tests Nasal scrapings were sterile Biopsy of one of the lesions showed the corium in the center of the section to be granulomatous, consisting of pale mononuclear cells, some with foamy cytoplasm, and a small number of lymphocytes Occasional fibroblasts were present in the periphery of the lesion The character of the granuloma was identical with the leprous lesions from our material at the hospital, but no acid-fast bacilli were found in the section with Fite stain (Dr Vero Dolgopol)

left cubital region On diascopic pressure there is no change in intensity of color

He is overweight His height is 5 feet and 5¾ inches (164 4 cm), and he weighs 172 pounds (78 2 Kg) stripped The abdomen is pendulous The breasts are prominent and the nipples retracted The genitals are small for his age Scrapings of the patches in the cubital region and axillas were negative for tinea on direct examination and culture

A histologic section taken from a hyperpigmented lesion on the neck according to Dr Charles F Sims showed the features of acanthosis nigricans for the most part, except for the absence of pigment He suggested that avitaminosis A be considered He stated that the epidermis was verrucous The granular layer was in part thickened and in part thinned, and at one or two points absent The epidermis was moderately and irregularly acanthotic with considerable interlacing of the rete pegs The basal margin did not present much pigment, as suggested by the clinical diagnosis There was a diffuse reaction in the papillary zone and a perivascular one in the subpapillary zone composed of small round cells, wandering connective tissue cells and scattered chromatophores Some interstitial and parenchymatous edema of the papillary zone were observed

DISCUSSION

DR HENRY E MICHELSON (by invitation) One reads in the literature of children with acanthosis nigricans occasionally experiencing something like the Cushing syndrome, but I think that the lesions of children with this disease will heal without any trouble

DR HOWARD FOX The opinions that these lesions are benign are different from those expressed at the last meeting At that time, some members stated the opinion that some of these cases terminate fatally

DR HANS J SCHWARTZ The case that I reported some time ago was not of the juvenile type The patient was followed up at the Memorial and New York hospitals and died at the age of 53 years The case had been regarded as one of juvenile acanthosis nigricans, but autopsy showed an enlarged liver which proved to be carcinomatous

DR WILLIAM CURTH (by invitation) I think that most of these cases of benign diseases continue without becoming cancerous In the cases of malignant disease there can be an interval of eight to ten years between the appearance of the cutaneous lesions and the manifestation of the cancer

DR FRED WISE The consensus is that in these juvenile cases as a rule complications do not develop, but the patients have to be kept under observation until they reach maturity and adulthood

A Case for Diagnosis (Dermatitis Factitia of Both Feet) Presented by DR EUGENE F TRAUB

Rosacea-like Tuberculid of Lewandowsky Presented by DR FRED WISE

Tuberculous Ulcerative and Fungoid Lesions of Buttocks and Perineum Presented by DR FRED WISE

Dr Jackson claimed that she isolated gram-positive, non-acid-fast forms from the cutaneous lesions It is interesting to note that this patient, though exposed to acute contagious diseases while at the hospital, did not become infected with any of them

DISCUSSION

Dr Gerald F Machacek I saw the child several months ago and suggested treatment with streptomycin with hesitation, as this is a "benign" form of leprosy

Dr Frederick Reiss (by invitation) I believe this case is one of typical minor tuberculoid leprosy

Dr A Benson Cannon I suggest that the patient be treated with diasone® by mouth, beginning with small doses and gradually increasing the dosage Dr Faget reports excellent results in the treatment of leprosy with that drug and states that it is less toxic than other preparations He states that the patient must take the medicine for six months or longer before improvement can be noticed

Dr Maurice J Costello I have tried streptomycin in cases of this disease, without the slightest benefit

Granuloma Inguinale of the Mouth and Genitalia Presented by Dr A Benson Cannon

E S, a Puerto Rican woman aged 26 who has been in the United States for six years, was admitted to the City Hospital on Jan 9, 1947, complaining of sores in the mucous membranes of the mouth, lips and anal-genital region of twelve months' duration The patient has been separated from her husband for five years She has never been pregnant. The past and family histories are essentially noncontributory

The present disease began with a small ulcer near the anus twelve months ago, which gradually increased in size, spreading around the anus and the crotch to the front and involving the inguinal regions and the vulva with an extensive ulceration which is painful on motion

Note—Donovan bodies were subsequently found in the oral lesions and also in the genitocrural ulcer The patient was given three small blood transfusions of 250 cc each and an injection of fuadin® every day The improvement has been spectacular There was immediate relief from pain, so that the patient eats well, can walk and has gained 20 pounds (9 1 kg) in weight On February 24 most of the oral lesions were gone and those in the groin were noticeably better Of the last 65 patients with granuloma inguinale admitted to hospitals, this is the second to have lesions of the oral cavity

Fox-Fordyce Disease Alopecia Areata Presented by Dr George C Andrews

R M W, a Negro woman aged 20, single, is presented from the Vanderbilt Clinic She was first seen in October 1946, with a pruritic eruption of one year's duration, which had appeared after taking injections from her private physician to "stimulate hair growth" Episodes of partial loss of hair had recurred over a period of ten years The eruption began in the axillas and had spread to involve other areas There has been no exacerbation at the time of the menses, which have been regular until the past month, when a mild metrorrhagia occurred

Eugene F Traub, M D, *President*
George M Lewis, M D, *Secretary*
Nov 26, 1946

Lupus Erythematosus Presented by DR ANTHONY C CIPOLLARO

R P, a boy aged 3, was first seen by me on Nov 15, 1946, with an eruption on the face which the mother thought followed mosquito bites The eruption appeared on both cheeks and finally spread across the nose After about two weeks the child was taken to the Skin and Cancer Unit, where a blood cell count, tuberculin tests and a biopsy were performed

The blood cell count showed mild secondary anemia The reactions to tuberculin tests were negative in dilutions of 1 1,000,000, 1 500,000 and 1 100,000 The report of biopsy of the right ear lobe was "inflammatory phase of lupus erythematosus"

The patient now presents an erythematous eruption involving both cheeks and most of the nose The shape of the eruption roughly resembles a butterfly There are telangiectatic vessels, and the scales are dry and adherent The lesions are sharply demarcated

Iodized salt was prescribed and the application of a sulfur preparation to the affected areas Within two weeks the eruption improved at least 75 per cent

DISCUSSION

DR PAUL E BECHET There is no doubt that the location is the usual one for lupus erythematosus and the scaling is characteristic, but the eruption lacks the follicular keratoses that one sees in the discoid type of lupus erythematosus This may be explained by the fact that the skin of young children is less apt to have keratotic lesions than the skin of adults I agree with the diagnosis The interesting thing is the age of the patient It seems to me that the incidence of lupus erythematosus in young children is greater today than it was years ago, and I believe that this is due to the increased tendency to exposure to the sun

DR RAY H RULISON I think that it is lupus erythematosus, probably of a superficial type

DR HOWARD FOX I agree with the diagnosis, particularly because histologic examination of one of the lesions confirmed it I do not agree with Dr Bechet that this disease is frequently seen in children It is most extraordinary to see 2 cases in babies at one meeting At least, it has never happened in my experience

DR GERALD F MACHACEK I do not know what else I would call this but lupus erythematosus Several years ago I saw 2 fairly well nourished children of this age group with lesions that were not as scaly as these but had the same distribution and also developed after exposure to sunlight The diagnosis was lupus erythematosus These children were on a diet of bananas, but appeared well nourished I do not know what ultimately happened, but I understand that they improved after the diet was varied The only clinical diagnosis I could make in the case presented by Dr Cipollaro would be lupus erythematosus, but I should consider the possibility that it might be due to or precipitated by some dietary imbalance, perhaps avitaminosis

DR A BENSON CANNON I agree with Dr Fox that lupus erythematosus in infants must be an exceedingly rare disease I do not recall having seen a typical

There are many areas of alopecia in the occipital region of the scalp An eruption consisting of discrete conical papules is present over the lower mandibular region and on the sides of the neck, axillas, breasts and periumbilical, pubic and perianal regions Secondary lichenification is present

Histologic examination of tissue from between the breasts was consistent with a diagnosis of Fox-Fordyce disease A second biopsy has recently been made of material taken from the side of the neck, but the results have not yet been reported

Treatment has consisted of antipruritic agents locally, and administration of roentgen rays, which gave only temporary relief Pyribenzamine® and benadryl® have been given since Dec 16, 1946, and the patient has experienced considerable relief since the dosage has been increased to 100 mg of pyribenzamine® three times daily with 100 mg of benadryl® at bedtime

DISCUSSION

DR A BENSON CANNON This patient was presented at the Vanderbilt Clinic conference, and the consensus of the group was that while the eruption might be that of Fox-Fordyce disease it was certainly most atypical While the lesions in the axillas did simulate Fox-Fordyce disease, there was so much lichenification of the skin and the eruption was so widespread on the neck, chest and abdomen, where no apocrine glands are supposed to exist, that one should suspect an additional dermatitis probably caused by treatment I think that benadryl® is most beneficial in relieving highly nervous patients, and especially those with pruritus, but I doubt whether it has any desensitizing effect in allergic states There is an increasing number of reports of unfavorable reactions and even addiction to benadryl,® so that one should be cautious in prescribing it, especially over long periods

DR GEORGE M LEWIS I should like to suggest the diagnosis of alopecia marginalis

DR MAURICE J COSTELLO We see Negro women at Bellevue Hospital rather frequently who have this condition I think it is traumatic marginal alopecia They put up their hair at night in tight crimpers I have seen it in white women also who fix their hair in a similar manner and dress it in the so-called up-sweep fashion

DR GERALD F MACHACEK I am of the opinion that it is Fox-Fordyce disease The material taken for the second biopsy did not go deep enough to include the acini of the gland, but most of the pathologic change is around the outlets The first biopsy showed an apocrine gland and the neurodermatitic changes which I would not expect in Fox-Fordyce disease

Bowen's Disease (Two Large Lesions, One on the Shoulder and the Other on the Leg). Presented by DR MAURICE J COSTELLO

ALSO PRESENTED

A Case for Diagnosis (Tuberculosis?) Presented by DR EUGENE F TRAUB

Lymphocytoma Presented by DR GEORGE C ANDREWS

case of lupus erythematosus in a child under 3 years of age I think that it is necessary to observe such an eruption for some months and to have a biopsy made before one can be certain of the diagnosis of lupus erythematosus in infants Recently a baby was admitted to the hospital with the diagnosis of lupus erythematosus, but it proved to be infantile eczema In the case presented, the location and character of the lesions suggest the diagnosis of lupus erythematosus and the report of biopsy supports that diagnosis I should suggest, however, that the patient be observed longer and that another biopsy be made

DR JOHN C GRAHAM I think that it is lupus erythematosus, clinically at least I have never seen a similar case

DR MAURICE J COSTELLO I think that the patient has lupus erythematosus, and I think that it is the disseminated type, as there are lesions on the external surfaces of the forearms as well as on the face and neck It is the type of lupus erythematosus that will have to be watched carefully It would not be advisable to administer gold salts to this patient

DR FRANK C COMBES I agree with the diagnosis Of course, the youngster does look undernourished I agree with Dr Machacek, and there might also be an investigation as to tuberculosis in this family and in the child himself

DR GEORGE C ANDREWS The delicate character of this child's skin should be noted About two summers ago I saw 2 children, about 2 or 3 years of age, with lupus erythematosus One was in New York Hospital for a month under observation, and the diagnosis was well established These patients have both improved I have seen them within the past six months The improvement was great with proper diets, with a great deal of vitamins, wheat germ and injections of crude liver extract Both have slight traces of disease but are greatly improved They had the extensive discoid type of lesions on the face

DR NIELS DANBOLT, Oslo, Norway (by invitation) I agree with the diagnosis It is surprising to see lupus erythematosus in such small children I am of the opinion that you see more of this disease here than we do in Norway I can not understand why you use the name "lupus" In Scandinavia we have dropped that misleading term altogether and call it just "erythematodes"

DR GEORGE M LEWIS From the clinical features presented, I would favor lupus erythematosus over other diseases with which the disease could be confused

DR EUGENE F TRAUB My co-workers and I saw this patient at the New York Skin and Cancer Unit several months ago, within a short time following his summer exposure to sun He presented a classic type of discoid lupus erythematosus, and the features that were present then, namely, the dilated follicular plugs and what appeared to be superficial atrophy, are not so apparent now A biopsy was performed to confirm the diagnosis chiefly because of age of the patient

DR ANTHONY C CIPOLLARO I also thought that lupus erythematosus was extremely rare in children of 3 and under, and for that reason I am presenting 2 cases I think that the diagnosis has been well established in this case, both clinically and histologically, and I should also like to emphasize the improvement which followed treatment with iodized salt

Lupus Erythematosus Presented by DR ANTHONY C CIPOLLARO

M Z, a girl aged 19 months, born in the United States, was first seen by me on July 25, 1946 The mother first noticed a rash on the right cheek when the

Psoriasis and Pustular Psoriasis Presented by DR GEORGE M LEWIS

A Case for Diagnosis (Hypostatic Eczema? Purpura? Kaposi's Sarcoma?) Presented by DR MAURICE J COSTELLO

Tinea Capitis in a 16 Year Old Girl (Previously Presented at the Manhattan Dermatologic Society Oct 8, 1946) Presented by DR ANTHONY C CIPOLLARO

Scleroderma, Generalized Presented by DR EUGENE F TRAUB

Psoriasis Toxic Eruption Secondary to Dermatophytosis Blue Nevus Presented by DR EUGENE F TRAUB

Kaposi's Sarcoma Resembling Granuloma Pyogenicum Presented by DR ANTHONY C CIPOLLARO

Tertiary Syphilis Presented by DR MAURICE J COSTELLO

Eugene F Traub, M D, *President*

George M Lewis, M D, *Secretary*

Feb 25, 1947

Ulcer (Postdesiccative, Left Thumb) Xeroderma Acarophobia Neurotic Excoriations Presented by DR GEORGE M LEWIS

A Case for Diagnosis (Behcet's Syndrome? Pemphigus? Leukemia Cutis?) Presented by DR EUGENE F TRAUB

I M, a man aged 52, has been previously presented He was first seen at the Skin Clinic of the New York Post-Graduate Hospital in 1930 when on otolaryngologic examination bullous lesions were discovered on his palate About the same time the patient noticed a sensation of stiffness of the upper lip He then reported to my office, where he has since been a private patient

On Aug 7, 1931, the patient presented an ulcerative lesion on the roof of the mouth, of long duration, which finally healed after wide endotherm removal In 1932, erythematous, scaly lesions appeared on the upper lip and in both nasolabial folds Tonsillectomy was performed Apart from the period 1932-1934, during which time the patient was entirely free of lesions, there was a continuous appearance of lesions in the mouth and buccal mucosa, as well as on the mucosa of the hard and soft palate, together with erythematous, scaly, psoriasiform lesions on the lips, nasolabial folds, eyebrows and penis

On the buccal mucosa at present there are several rounded, denuded areas about 1 to 1 5 cm in diameter The uvula is thickened and shows small ulcerations There are ill defined, confluent, polycyclically outlined ulcerations on the eyebrows, lips and glans penis, with flat, necrotic, scaling, moderately infiltrated, erythematous lesions The region around the chin is diffusely involved by a brown-red, scaly, infiltrated erythema

Results of urinalysis and Wassermann tests of the blood on many occasions have been negative, as were smears for Vincent's organisms and cultures for

baby was 3 months old, and since then it has spread persistently, without remissions, up to its present extent About four months ago lesions appeared on both forearms The child is decidedly undersized At the age of 15 months she weighed only 13 pounds (6 Kg) The baby was born without complications, and there were no unusual symptoms either before or after delivery

The patient presents an erythematous eruption involving both malar regions and extending across the bridge of the nose There are telangiectatic vessels and dry adherent scales, and the lesions are sharply demarcated There is one small lesion on the scalp and one small patch on each forearm A biopsy was not performed The patient was seen by me once, and then not again until the present time

Bismuth compound injections were advised, but the baby's pediatrician had read of the toxic effects of bismuth, causing death in 1 case, and he was therefore hesitant about using it Injections of crude liver extract were then recommended

DISCUSSION

DR GEORGE C ANDREWS I agree with the clinical diagnosis, although I am not as positive as in the other case I should like to call attention again to the fact that the child's skin is delicate and different from that of the mother, who has a coarse skin That was true in my 2 cases

DR FRANK C COMBES I agree with the diagnosis and think it represents a remarkable improvement

DR MAURICE J COSTELLO I question the diagnosis This child must have some developmental defect which also affects the skin She does not appear to be a sick child I think that it is a cutaneous manifestation of a developmental defect, such as the telangiectatic type of streaking seen in some major ectodermal congenital defects

DR J GARDNER HOPKINS I could not see much reason for calling it lupus erythematosus except for the involvement of the flush areas I saw no follicular plugging or hyperkeratoses There was a lesion in the elbow flexure which was eczematous, and I wondered whether it were not infantile eczema

DR A BENSON CANNON I agree with Dr Costello and Dr Hopkins that the eruption looks more like infantile eczema than lupus erythematosus The lesions are too diffuse, red, swollen and exudative for lupus erythematosus A further study of the case, including a biopsy, might help to make the diagnosis

DR GERALD F MACHACEK I am less inclined to accept this as lupus erythematosus in view of the inanition and general underdevelopment My previous remarks are even more applicable to this case

DR HOWARD FOX I agree that it is difficult to make a diagnosis in a child who is as restless as this one was The fact that the eruption began when the child was 3 months old makes it an exceedingly rare case of lupus erythematosus, if it is that disease The obvious developmental defect may have something to do with this eruption

DR RAY H RULISON Aside from the distribution, I did not find much evidence to warrant a diagnosis of lupus erythematosus

DR EUGENE F TRAUB If we are to accept this as a case of lupus erythematosus, it would have to fit into the acute disseminated type, because the patient certainly does not present any of the characteristics of the discoid type As a matter of fact, Dr Hopkins and the others are probably correct in their feeling

Monilia Results of roentgen examination of the chest, gallbladder and gastrointestinal tract were essentially normal except for a suggestion of periduodenitis and colonic hypermotility with general irritability and spasm The result of cystoscopic examination was negative for infection or tumor The results of Pels' tests on three occasions were positive

Ophthalmologic examination has shown chronic blepharokeratoconjunctivitis of unknown cause, which has recurred about every three months Topical application of penicillin has produced only temporary improvement

Blood cell counts have shown leukocytosis, with the count varying from 8,200 in 1933 to 23,500 in September 1946, with lymphocytes varying from 35 to 82 per cent

Treatment has included vitamins, acetarsone, and sulfonamide drugs given orally, with parenteral administration of neoarsphenamine, oxophenarsine hydrochloride, bismuth compound, liver, eschatin® (an extract of the adrenal cortex), moccasin venom, autogenous mixed vaccine, penicillin and typhoid vaccine and autohemotherapy His condition is essentially unchanged

DISCUSSION

DR HOWARD FOX I think that Dr Traub's suggestion of Behcet's syndrome is correct The eruption involves the three favorite areas of this disease, namely, the mouth, eyes and genitalia The disease has been extremely chronic, as it always is, and treatment has been of no permanent benefit Dr Traub has been persistent for seventeen years in trying various methods of treatment, without success

DR A BENSON CANNON This is one of the most interesting cases I have seen for a long while, and I cannot offer any better suggestion than has already been brought forward I would classify the case as one of lymphoblastoma I believe that the location of the lesions is common in leukemia, and their infiltration, the deep, verrucous ulceration on the palate and the blood cell counts would cause me to think of leukemia rather than any other form of lymphoblastoma I should suggest that another biopsy be made of the skin and one of the ulcer on the palate and that the blood and bone marrow be studied by a hematologist The slowly progressive nature of the disease, the increased total white blood cell count and lymphocyte count indicate a bad prognosis Leukemic states can last for years

DR GERALD F MACHACEK My conception of Behcet's disease is that it is a condition which recurs and is essentially vesicular The infiltration on the face makes me agree with Dr Cannon that leukemia is certainly one of the differential diagnoses that must be considered I would also suggest that the presenter check the history again to ascertain whether the patient is not taking phenolphthalein in some occult form

DR J GARDNER HOPKINS I believe that the lesions of Behcet's syndrome are ulcerations resembling aphthae This man's lesions on the penis have never ulcerated The ulcerations described by Behcet do not extend in a serpiginous manner as the lesion on the palate has done in this case Dr Cannon's suggestion that this is leukemia seems more plausible, though it is a little difficult to reconcile with the history that thirteen years ago he had a chronic ulceration on the cheek without blood changes

DR. GEORGE C ANDREWS I do not think that it is Behcet's syndrome Iritis and hypopion are not present The lesions in Behcet's syndrome, as Dr Hopkins

that this patient may not have lupus erythematosus at all, but that the hyperactivity of this child may be responsible for some of her cutaneous lesions It appears that the child rubs the face and in this manner brings about some, if not all, of the erythema and irritation The lesion on the flexor surface of the forearm is definitely edematous and vesicular and suggests either a patch of eczema or possibly even an artefact My suggestion would be for Dr Cipollaro to hospitalize the child and restrict the motions in such a way that she cannot rub her face or roll the head on the pillow and observe whether this does not cause an amelioration of the symptoms

DR ANTHONY C CIPOLLARO My diagnosis is based on two hasty observations When I saw the child the first time, I thought of several diagnoses, such as developmental defect, psoriasis, eczema and lupus erythematosus In favor of lupus erythematosus are the persistence, steady spreading, demarcation, dry adherent scales, absence of remissions and lack of vesiculation The child's pediatrician has never thought of eczema in this case The diet has been carefully supervised There is no history of atopy in the family. It is true that I did not find keratotic plugs, but in a child with a delicate skin one does not expect to find the same degree of scaliness or follicular plugging as in an adult Against eczema is the lack of vesiculation and crust formation As far as developmental defects are concerned, I could not see any evidences of nevus flammeus, and it is not like any other developmental defect I know I think that the fact that the mother is small has a good deal to do with the child's small size The evidence as I see it favors a diagnosis of lupus erythematosus I shall discuss the question of performing a biopsy with the pediatrician, and if he and the mother consent, I shall proceed with biopsy

Chronic Discoid and Lichenoid Dermatosis Presented by DR GEORGE C ANDREWS

J G, a Jewish man aged 50, was first seen Oct 9, 1946, with an eruption which had had its onset fifteen years previously, beginning with a small lesion on his thigh This had spread gradually The dermatitis had cleared with roentgen therapy, ultraviolet irradiation and various injections Exacerbations occurred at intervals but responded with the described treatment The patient has noticed also that healing occurred spontaneously during vacations in Florida There was a history of eczema during infancy Allergy testing in 1931 revealed a positive reaction only to orris root

Examination shows a patchy, vesicular, papular, erythematous discoid and lichenoid dermatitis on the body and particularly on the extremities and penis

A complete blood cell count revealed 96 per cent hemoglobin, 4,720,000 red blood cells and 5,850 leukocytes The differential smear showed 16 per cent eosinophils The urine was normal

The patient has shown no improvement with the parenteral use of penicillin, oral use of sulfapyridine, an elimination diet or arsenic trioxide solution given intramuscularly Local treatment has consisted of mild antipruritic applications and superficial roentgen therapy

DISCUSSION

DR FRANK C COMBES This man presents practically all of the characteristics one usually associates with this disease In all cases the question comes up as to

DISCUSSION

DR EUGENE F TRAUB Clinically this is not a case of pseudoxanthoma elasticum, because, in addition to being more yellowish, this disease tends to run in transverse striations along the neck and the lesions, while slightly elevated, appear to be atrophic I do not believe that the patient has poikiloderma of Civatte The characteristic telangiectatic vessels, recticulated network, small papules and peculiar pigmentation accompanying that disease are lacking here I agree that this patient has some changes which suggest either scleroderma or dermatomyositis, and there are some deep-seated, thickened rather than atrophic lesions present The patient should be studied further

Psoriasis, Granuloma Annulare, Urticaria Presented by DR ANTHONY C CIPOLLARO

Atopic Eczema, Congenital Abnormalities, Vascular Nevus, Elephantiasis, Undescended Testes Presented by DR EUGENE F TRAUB

Chronic Lupus Erythematosus (with Associated [?] Deafness) Presented by DR GEORGE M LEWIS

Infected Preauricular Branchial Cysts Presented by DR MAURICE J COSTELLO

T B, a boy aged 15, has in the preauricular regions two nearly dime-sized, slightly elevated, red, somewhat infiltrated lesions In the center of each is a tiny hole from which pus exudes on slight pressure Above and posterior to these are two oval indentations measuring about 3 mm, located at the root of the helix The latter are seen from time to time in persons with or without other congenital anomalies They are often familial They are the upper openings of the partially obliterated branchial clefts The explanation of the sinus openings is that the purulent material in these cysts drains by gravity through the skin in these locations The patient has been referred to an otolaryngologist for excision of the cysts

DISCUSSION

DR HOWARD FOX I agree with the diagnosis This infection did not go through the normal channel, and it caused an impetiginous patch where it broke through the skin

DR GERALD F MACHACEK Cancers are known to arise in branchial clefts Oncologists place special emphasis on this observation

DR EUGENE F TRAUB Injections of iodized poppyseed oil might cause trouble The tract may go much further or branch off in a different direction than is taken by the oil, so that a false impression might be obtained In addition, there are other complications from this process that render it inadvisable

DR GERALD F MACHACEK I have seen iodized poppyseed oil forced into tissue with the resultant formation of granulomas which look like sarcoids but are really similar to paraffinomas

Bullae of Epidermolysis Bullosa Occurring on a Vaccination Site Presented by DR MAURICE J COSTELLO

Mrs S B, aged 70, from the Bellevue Hospital outpatient department, was vaccinated in the left deltoid region April 14, 1947 A week later a dime-sized

whether this is a definite disease entity I think that we have seen enough cases now to justify its distinction from other dermatoses which it simulates I was interested to know that the man did not respond well to sulfapyridine We have had several patients who had good remissions definitely related to the administration of that drug

DR MAURICE J COSTELLO The only therapy I can think of which has not been tried is nonspecific therapy with triple typhoid vaccine injected intravenously I think that it would be beneficial, especially if combined with sunlight and salt water bathing, preferably in a southern climate

DR A BENSON CANNON The diagnosis of chronic discoid and lichenoid dermatosis had never occurred to me The patient is a wealthy business man with a happy disposition He has consulted me at infrequent intervals since 1933 for various minor dermatologic complaints Three years ago, I saw him for a few macular, pea-sized to five-cent-piece-sized, round to oval, scaly and crusted patches that were slightly itchy I diagnosed it as an eczematoid dermatitis due, probably, to a local irritant The lesions cleared with a few fractional doses of roentgen rays and tar ointment Since that time I have seen him every few months for a recurrence of the lesions, and there were never more than a couple of dozen After taking ocean baths in Florida and being in the sun, the patient noticed that all lesions disappeared, but these returned a few months after his return to New York Cultures for fungi were negative Patch tests elicited a strong reaction to pyrethrum, tar, phenol salicylate ointment, sulfur and several soaps Itching was never a pronounced symptom, and the lesions were always of the same character—macular, exudative, crusted areas There were never any nodules, plaques, pigmentation, lesions of the glans penis or adenopathy, symptoms that are usually found in chronic discoid and lichenoid dermatitis Tonight the patient presents many more lesions than I have observed before, but even now they are of the eczematous and crusting type

DR GERALD F MACHACEK I am of the opinion that many persons suffering from so-called chronic discoid and lichenoid dermatosis also suffer from an element of contact hypersensitivity and an element of cutaneous infection Recently in a biopsy in such a case I found a curious change in the coil glands, which appeared to be hypertrophic The inflammatory reaction seemed to reach well down into the secreting element of the gland

DR GEORGE C ANDREWS This man came to me in October, when he was worse than he is today At that time the lesions were widespread and oozing, and he was in a miserable condition He had been in Florida and knew the eruption would clear up if he went there again He said that the eruption came in cycles He is unmarried and worries a great deal He is in the textile business I have talked with his employer There is not much doubt in my mind that this is a case of chronic discoid and lichenoid dermatosis Dr Sulzberger examined him and agreed It interests me that he handles textiles, because I have another patient, a man who is a cotton goods salesman, and I know that Dr Sharlit had a patient sensitive to silk I have performed patch tests with cotton, rayon and silk, and all results were negative

DR EUGENE F TRAUB I should like the presenter to explain why these patients, particularly this one, appear to have been benefited by the warm climate Does he get anything by such a change except removal from his environment?

vaccination "take" developed, surrounded by a palm-sized area of erythema and edema The following day two marble-sized, thick-walled, tense bullae appeared on either side of the vaccination These are diagnosed as bullae of epidermolysis bullosa occurring on a site of edema and erythema and probably caused by trauma, such as scratching They were not secondary vaccination inoculations The patient has epidermolysis bullosa of the acquired type for which she has been treated for some months in the clinic Typical lesions of the disease were found on the nails, elbows, knees and other points of trauma

DISCUSSION

DR HOWARD FOX The patient shows signs of epidermolysis bullosa of the nails It does not seem like a spread of the vaccination or autoinoculation The lesions are in a region which has been more or less traumatized, and one should accept the possibility that these bullae are part of her old disease

DR PAUL E BECHET I agree with the diagnosis The trauma involved in the performance of a vaccination is enough to cause an extension of lesions of epidermolysis bullosa, which is precipitated in any location by trauma

DR RAY H RULISON I agree with the diagnosis, and I agree with Dr Combes that the trauma arises not from the superficial scarification but from the virus I can readily see how irritation and infiltration would precipitate lesions in a patient with this disease, but I have seen almost as severe reactions in persons without this disorder

DR JOHN C GRAHAM I do not quite agree with Dr Combes that scratching could not cause the lesions If her vaccination itches as mine does, she could get the blebs of epidermolysis bullosa from scratching I think that she has traumatized it

DR EUGENE F TRAUB This could well be an example of a dystrophic type of epidermolysis, and in that type particularly blisters will appear spontaneously and with the least provocation I feel that this insult was more than adequate to cause such a change and agree that vaccination was responsible

Neurofibromatosis, Ichthyosis Presented by DR GEORGE M LEWIS

Dermatitis Medicamentosa (Demerol®), Addisonian Pigmentation (Arsenical Keratosis and Pigmentation?) Presented by DR GEORGE M LEWIS

A A, a man aged 45, a former taxicab driver, had minimal pulmonary tuberculosis five years ago Two years ago a diagnosis of Addison's disease was made at the New York Hospital, and this has been treated with 6 Gm of salt and 4 Gm of desoxycorticosterone acetate daily One year ago keratotic lesions on the palms and soles were first noted Two months ago the patient had severe neuritic pains in the legs, for which he has been taking 50 mg of meperidine hydrochloride (demerol®) daily About three weeks ago a pruritic, burning, erythematous, diffuse eruption developed on the extremities and later on the trunk, and this eruption soon became dry and scaling There is no obtainable history of arsenic ingestion

A diffuse, erythematous, dry, scaling eruption over the extremities and trunk is present There are keratotic lesions on the palms and soles, and keratotic

DR GERALD F MACHACEK It is my impression that a number of the patients that Dr Cannon sent to Texas were persons who handled textiles, and particularly tailors who handled dirty garments

DR GEORGE C ANDREWS My other patient was in Presbyterian Hospital for several months and was seen in consultation by Dr MacKee, who agreed with the diagnosis of chronic discoid and lichenoid dermatosis The eruption cleared up temporarily after electric shock treatments He stayed well for about three weeks and then started worrying, and the eruption recurred He went to a doctor in New Jersey who continued shock treatments and telephoned me that the man was completely cured I said that I would like to hear from him again in about six months Later he told me that the patient was again ill There is certainly a large psychic element in this disease

Knuckle Pads Presented by DR J GARDNER HOPKINS

E M, a married woman aged 40, presents thickening of the skin over the proximal interphalangeal joints of all fingers, but not of the thumbs or toes These have gradually developed over a period of eighteen months There have been no subjective sensations The patient works as a secretary and office nurse There is no history of injury or of rheumatic fever

The lesions form disks 10 to 15 mm in diameter These are firm, inelastic and apparently formed by thickening in the cutis or subcutis without notable epidermal change

Roentgen examination showed no changes in the bones Biopsy showed dense collagen with some evidence of degeneration but no characteristics on which to base a diagnosis

DISCUSSION

DR FRANK C COMBES The only treatment I know of is protective—the lesions should be covered with elastoplast for several months Knuckle pads do not respond well to irradiation

DR MAURICE J COSTELLO This woman has knuckle pads on the second, third and fourth fingers, but none on the thumb I think that if her household activities were carefully studied one could find the cause

DR HOWARD FOX I agree with the diagnosis, but I do not know of any treatment that cures the disease We talk the problem over perennially and get nowhere, except that we agree that none of us has ever seen a case in which it could be proved that trauma was causative

DR RAY H RULISON Some patients have Dupuytren's contracture, which is apparently not a part of the picture and yet it does occur later in some cases

DR GEORGE M LEWIS In a patient with a rather typical lesion temporary improvement was obtained by the use of moleskin adhesive plaster, continuously applied, as first advocated by Kest Moleskin seems more effective than ordinary adhesive plaster

A Case for Diagnosis (Pemphigus Vulgaris? Dermatitis Factitia?) Presented by DR GEORGE C ANDREWS

A Case for Diagnosis (Dermatophytosis? Pustular Psoriasis? Bacterid?) Presented by DR EUGENE F TRAUB

lesions arise from the skin of the body, especially on the shoulders Many pigmented brown macules are present, especially on the back and shoulders

A complete blood cell count showed 4,400,000 red blood cells, 3,800 white blood cells and 13 Gm hemoglobin, with 59 lymphocytes, 7 monocytes, 14 eosinophils, 20 polymorphonuclear leukocytes (mature forms 16 and band forms 4) Blood sodium was 325, potassium 16 25, and cholesterol 185 mg Results of biopsies have not been reported

DISCUSSION

DR HOWARD FOX This man has a striking and profuse pigmentary eruption As the pigment is in the form of small macules and not a diffuse pigmentation, it is certainly not typical of Addison's disease and looks more like arsenical pigmentation Arsenic, however, does not produce pigment in the mouth, whereas Addison's disease does, and there is one small pigmentary patch opposite one of the patient's molars I still think that the whole picture is probably one of arsenical pigmentation

DR PAUL E BECHET There is no dermatologic condition I know of that presents this picture of lentiginous pigmentation, particularly on the shoulder blades The few patients with Addison's disease I have seen show more diffuse pigment, with generalized bronzing The patient does not have the dry skin and furfuraceous scaling so common in arsenical dermatoses

DR RAY H RULISON If this case had been presented as one of arsenical pigmentation and keratosis, with no history of Addison's disease, I think that one would accept it without question However, this case has been carefully studied, and, as I understand it, the patient has never been given arsenic and no excessive arsenic has so far been found If this man has Addison's disease I do not believe that it is fair to say that he must have arsenic retention and that the pigmentary changes are due to that, because they conceivably could be Arsenic should not be part of the diagnosis until it has been demonstrated

DR JOHN C GRAHAM Could the amount of treatment he has had affect his pigment?

DR GERALD F MACHACEK Pigmentary changes in Addison's disease need not be characteristic I saw photographs of patients with Addison's disease that curiously showed leukoderma Dr Potelunas tells me that the patient was admitted to the hospital in a crisis at one time

Eugene F Traub, M D, *President*

George M Lewis, M D, *Secretary*

May 27, 1947

Cavernous Hemangioma (Angioma Venosum Racemosum) Presented by DR MAURICE J COSTELLO

Hairy Nevus of the Scalp Presented by DR FRED WISE

A Case for Diagnosis (Parapsoriasis? Iododerma?) Presented by DR PAUL E BECHET

DISCUSSION

DR ROBERT BARTON, Dubuque, Iowa (by invitation) Since 1946 at the Chicago Intensive Treatment Center 9 patients with granuloma inguinale have been treated with streptomycin In every case the lesions disappeared within forty-five days after treatment was instituted In 3 of the cases there have been relapses Streptomycin as my co-workers and I have used it may or may not cure granuloma inguinale, but to date it is the most effective drug for that disease The pattern in Dr Ebert's case conforms to that in ours After treatment was stopped the lesions continued to heal without additional therapy The patients returned perhaps a month or two later with the lesions completely gone It appears that once treatment is given, the effects are protracted

Werner's Syndrome (Progeria of Adults) Presented by DR T CORNBLEET and (by invitation) DR D COHEN and DR J GRAFFIN

Pigmented Purpuric Lichenoid Dermatitis Presented by DR T CORNBLEET and (by invitation) DR D COHEN and DR N L BAKER

T B, a white man aged 30, has had purplish spots on the legs and dorsum of the feet for two years These are asymptomatic In January 1945 the right testis and epididymis were removed because of tuberculosis

On both legs, mainly on the anterior aspect, there are lichenoid purpuric papules Similar lesions are present on the dorsa of the feet, in groups There are pigmented macules, 2 to 5 mm in diameter, among the papules of the legs and dorsa of the feet

Roentgenogram of the chest reveals a soft fuzzy infiltration in the right apex Biopsy by Dr Caro showed Gougerot-Bloom's disease

DISCUSSION

DR H E MICHELSON, Minneapolis Pautrier said that if we wish to advance dermatology, it would be well if we eliminated ten names a year instead of adding ten new ones Following his suggestion, I would like to eliminate the name Gougerot-Bloom's disease now Sooner or later, we must decide that all of these diseases that are characterized by localized hemosiderosis are one and the same thing and differ only in their extent and their localization Gracing them with long names is one of the troubles that dermatology has had to contend with for many years

Scrofuloderma, Pott's Disease and Retrosternal Abscess Presented by DR T CORNBLEET and (by invitation) DR H SCHORR and DR N L BAKER

A Case for Diagnosis (von Recklinghausen's Disease?) Presented by DR I M FELSHER, DR JULIUS E GINSBERG, DR A SLEPYAN and (by invitation) DR I EIRINBERG

Mrs L P, a well nourished, well developed, Negro woman aged 49, was first seen at Mandel Clinic, Michael Reese Hospital, on May 15, 1947 On the left buttock and left thigh there are present two large, well circumscribed tumors measuring 4 5 by 3 inches (11 by 7 cm) and 7 by 3 inches (18 by 7 cm), respectively These tumors have been present since birth but have caused the patient no difficulty with the exception of occasional discomfort when pressure is applied

The tumors are extremely flaccid, lobulated and pendulous The skin covering them appears lighter and atrophic and at the periphery of the lesions is filled with giant comedos On palpation the lesions are firm and nodular

Microscopic sections taken from the edge and center of the lesion show hyperkeratosis, deep brown pigmentation of the basal layer, flattening of the rete processes and some hyperplastic sebaceous glands containing comedos The corium is replaced by a tumor mass of connective tissue cells containing many small blood vessels There are numerous mast cells present With the Van Gieson stain, the tumor tissue is essentially the same color as that of normal collagen The orcein stain shows absence of elastic fibers throughout the tumor



Lesions on the buttock and thigh of patient with diagnosis of von Recklinghausen's disease

Granuloma Fungoides, D'emblée Presented by DR THEODORE CORNBLEET

F S K, a white man aged 74, presents mushrooming tumors on the right wrist and posterior hair line Near the scalp lesion and on the left ear lobe there are several infiltrated plaques that are sharply outlined and of various sizes There is itching The lesions appeared eight months ago There were no preceding lesions of any kind or any itching The patient was in the hospital about the time of onset of the skin changes

Mycosis Fungoides Treated with Sodium Paraaminobenzoic Acid Presented by DR JAMES H MITCHELL

Mrs L McC, aged 52, was first seen on Jan 18, 1945, with a huge exuding tumor on the left ramus of the jaw There had been a generalized pruritic eruption for the past two years Various lesions of the type on the left cheek had appeared and had healed spontaneously with scarring

A clinical diagnosis of mycosis fungoides was made and confirmed by biopsy Intensive roentgen ray treatment was given to the point of tolerance on various occasions with good immediate response Intramuscular injections of chaulmestrol were begun on Jan 28, 1947, which were followed by an intense generalized toxic eruption

Pustular Psoriasis Presented by DR GEORGE M LEWIS

H J, a white woman aged 36, has had a recurrent pruritic vesiculopustular eruption on the soles for the past five years The pruritus is worse during the menses She was treated for three years with benzoic and salicylic acid (Whitfield's) ointment, aluminum acetate (Burow's) solution and ointment, boric acid and salicylic acid powders, naphthalan, ichthammol, crude coal tar, ammoniated mercury, sulfur, brilliant green, tannic acid, boric acid ointment and roentgenotherapy, with little if any improvement

When I first saw her, two years ago, penicillin ointment was used without success Thereafter for six months she was given intravenous injections of 1 per cent antimony potassium tartrate, supplemented with four fractional doses of roentgen rays and quinolor® ointment (a mixture of three chlorine derivatives of 8-hydroxyquinoline in a base of equal parts of petrolatum and wool fat) This therapy resulted in almost complete involution of the eruption The patient then used chrysarobin ointment and stannoxyl® (a combination of metallic tin and its oxide) tablets There was considerable improvement for several months, with only a few transient vesiculopustules and mild pruritus One year ago another exacerbation occurred Pyorrhea was treated at this time Results of roentgen examination of the teeth were normal The eruption gradually subsided, and the patient was free of lesions until three months ago, when the present relapse began A course of sulfadiazine, 4 Gm daily for two weeks, was given and an ointment containing resorcinol, salicylic acid and chrysarobin was prescribed

An extensive vesiculopustular eruption is present on the palms and soles The lesions are grouped in patches on the soles The nasal and oral cavities are normal, and there are no other evident foci of infection The result of urinalysis was normal, the Wassermann reaction of the blood was negative and cultures were negative for fungi

DISCUSSION

DR EUGENE F TRAUB I have tried antimony potassium tartrate, with the same results Dr Lewis reports temporary slight improvement followed by a return of the eruption I do not believe that it is possible to determine whether the tonsils are actually a focus in a given case even if pus is aspirated from them While it is certainly better to determine in advance that there is an infection in the tonsils, removing infected tonsils does not necessarily cure the eruption In 1 instance in which this was the case I discovered that the patient had an infection in his prostate which was thought to be secondary to the tonsillar infection Improvement followed prostatic massage

DR GEORGE M MACKEE According to histologic work that has been done recently, these conditions can be divided into two varieties One is psoriasis histologically, and the other is not Differentiation may make a therapeutic difference What was said about antimony potassium tartrate therapy is true about every possible treatment for this disease Everything tried has been successful only temporarily, except perhaps removal of foci of infection In spite of the fact that there is no cure, the majority of patients eventually recover

DR HOWARD FOX I agree with the presenter that it is proper to tell the patient, as Dr Andrews does, that it is not certain that he will get well after tonsillectomy, regardless of what organism is found on aspiration I should certainly suggest that this patient have her tonsils removed

Society Transactions

SAN FRANCISCO DERMATOLOGICAL SOCIETY

Ervin Epstein, M D, *President*

Frances M Keddie, M D., *Secretary-Treasurer*

April 26, 1946

A Case for Diagnosis (Thymoma). Presented by DR FRANCES A TORREY

Lymphoblastoma. Presented by DR FRANCES A TORREY

Lupus Erythematosus (Lichen Planus?) Presented by DR HIRAM E MILLER

C F S, a 56 year old white man, was first seen in the Dermatology Clinic of the University of California Hospital on Jan 7, 1946 He gave a history of a reddish scaly dermatitis on the face and neck for the past seventeen or eighteen years and of elevated purplish nodules on the backs of the hands for about one year

The physical examination revealed no abormalities A blood cell count and urine were reported normal The Kolmer and Kahn reactions were negative A fairly symmetric erythematous and scaly eruption involves the ears, nose and sides of the neck Whitish retiform lesions are present on the buccal mucosae, and the lips showed some deformity from atrophic scarring On the dorsa of the hands are groups of large, elevated, flat-topped and rounded violaceous papules

Biopsy specimens were obtained from the dorsum of the left hand and from the side of the neck Studies of a section from the neck showed slight parakeratosis and relative acanthosis The granular layer was prominent, and the basal cell layer of the rete pegs showed some liquefaction degeneration A fairly dense round cell infiltrate was present and was confined to the papillae and upper part of the cutis

The section from the dorsum of the hand showed prominent hyperkeratosis and an increased granular layer There were decided acanthosis with some liquefaction degeneration of the basal cell layer A moderately dense round cell infiltrate was present in the papillae and upper part of the cutis

Bismuth subsalicylate was given, 0 2 Gm intramuscularly weekly for a total of sixteen injections During this period there has been gradual regression of all cutaneous lesions

DISCUSSION

DR ERVIN EPSTEIN I had the opportunity of seeing this patient ten years ago in Los Angeles At that time he had typical lupus erythematosus on the nose and lips and no other lesions

DR. F G NOVY JR I agree with the diagnosis of lupus erythematosus

DR REES B REES I think that someone should point out the remarkable bandlike infiltrate in the sections from the hand and neck and the prominent

Psoriasis Following Smallpox Vaccination in a Seven Year Old Boy Presented by DR GEORGE M LEWIS

A Case for Diagnosis (Ulcus Vulvae Acutum of Lipschutz?) Presented by DR ANTHONY C CIPOLLARO

T L, a woman aged 35, first consulted me on Nov 15, 1946, because of recurrent ulcerative vulvar and oral lesions of eighteen months' duration The lesions began as small blisters and soon ulcerated The patient has used a number of remedies, but the lesions have continued to recur A month before consulting me the patient went to the Lahey Clinic for a complete medical check-up Her general physical examination was entirely normal except for slight obesity and the lesions of the mucous membranes of the mouth and vulva The result of the Hinton test was negative, and all laboratory studies gave normal results A smear from the vagina contained a moderate number of gram-negative bacilli, a few gram-positive bacilli and extracellular gram-negative diplococci No intracellular gram-negative diplococci were seen Smears from the mouth showed a moderate number of fusiform bacilli and gram-negative bacilli There were also a few gram-negative diplococci A positive diagnosis was not made, but the following diagnoses were considered Vincent's angina, aphthous stomatitis, Behcet's triple symptom complex, erythema multiforme, dermatitis herpetiformis and pemphigus

When I first saw the patient she had discrete pinhead-sized to pea-sized, deep, ulcerative lesions on the mucous membrane of the labia minora and some in the posterior part of the fourchet The mucous membrane surrounding and underlying the lesions was painful, red and somewhat edematous A few ulcerative lesions, much smaller and less severe, were seen in the mouth, and the gums appeared to be inflamed The tongue and the roof and floor of the mouth were essentially normal On clinical grounds the diagnosis of ulcus vulvae acutum was made There was no biopsy

The patient was treated with antiseptic solution, penicillin ointment and acetarsone and showed quick response There has been a recent exacerbation of the gums, and the patient was given vitamin C and riboflavin

She is presented for diagnosis and for suggestions regarding therapy

DISCUSSION

DR. A BENSON CANNON I suspect that the case is one of pemphigus Pemphigus sometimes remains limited to the mucous membranes for many months, and it is difficult to diagnose before it becomes generalized For example, a patient was admitted to the Vanderbilt Clinic several months ago with a severe, widespread, bullous eruption, conjunctivitis and lesions in the mouth and pharynx and on the labia, and a diagnosis of bullous erythema multiforme of the Stevens-Johnson type was made She now has typical pemphigus vulgaris with vegetating lesions Dr Cipollaro's patient is similar to the one I presented this afternoon The lack of pain and the number of lesions are against the diagnosis of ulcus vulvae acutum

DR FRED WISE It is difficult to make a definite diagnosis in cases of this kind, unless one has the opportunity of keeping the patient under observation for a long time Patients with a diagnosis of ulcus vulvae acutum sometimes have

follicular plugging in the epidermis There are some plasma cells in addition to small round cells

DR HARRY J TEMPLETON The lesions on his hands are deep violaceous and are thickened They are classic lesions of lichen planus hypertrophicus There may be two conditions

DR NORMAN EPSTEIN It is of interest that biopsy specimens from the hands and neck in this case are much alike Although the bandlike infiltrate in the upper part of the corium suggests lichen planus, the lesions on the face could hardly be anything but lupus erythematosus

DR ARNE E INGELS I agree, the sections verify that

DR HIRAM E MILLER I examined sections from this patient and made a diagnosis of lichen planus, but after examining the patient I feel reasonably certain that he does not have this disease The microscopic observation must be correlated with the clinical picture The patient certainly has lupus erythematosus on the face, and the lesions on the dorsa of the hands resemble lichen planus but could be, and probably are, lupus erythematosus The sections showed an increase in the granular layer, and the infiltrate was certainly bandlike The histologic changes are compatible with the diagnosis of lupus erythematosus, and the clinical appearance, I think, is also that of lupus erythematosus

A Case for Diagnosis (Necrotic Nodules on the Face?) Presented by DR ERVIN EPSTEIN

DISCUSSION

DR G V KULCHAR The diagnosis for the older woman of the 2 patients, I think, is factitious dermatitis, which is especially apparent from the linear scarring The disease of the other woman might be what is called pyoderma faciale

DR REES B REES I believe that both women have neurotic excoriations The case that Dr Kulchar discussed first is interesting and classic, because of the patient's elaborate description of the manipulation of her lesions

DR MERLIN T-R MAYNARD, San Jose, Calif I agree with the diagnosis of neurotic excoriations Both women admit picking and squeezing their skin The scars are typical of those produced by persistent manipulation I tried the pharyngeal reflexes in each of them Each has a rather active pharyngeal reflex

DR. ERVIN EPSTEIN The diagnosis of dermatitis factitia presupposes a method of producing the lesions These lesions started subcutaneously as hard nodules There is no question that the lesions have been altered mechanically, but I still find it difficult to believe that the lesions could be produced by any chemical, physical or mechanical agent

DR E J RINGROSE (by invitation) I think that these excoriations were produced by finger nails I believe that one should differentiate between neurotic excoriations, of which the lesions in these cases are typical, and dermatitis factitia produced by chemical or other destructive agents Have you not seen a primary lesion produced by pinching and squeezing?

DR E K STRATTON I think that these patients can be helped by a psychiatrist if they wish to be helped However, most of them are not willing to cooperate I believe that in any event they belong in the office of a psychiatrist and not in the office of a dermatologist

remissions and exacerbations over a period of several years, and the condition is resistant to therapy

DR EUGENE F TRAUB Does the patient take aminopyrine?

DR ANTHONY C CIPOLLARO She does not take any medicine A culture for Monilia was made at the Lahey clinic, and it was negative I considered pemphigus, as did some of the men at the Lahey Clinic, but thus far she has had no more manifestations than she showed tonight I shall have to observe her further

Multiple Vaccination of the Face (from Barber Shop?) Presented by DR EUGENE F TRAUB

G R, a man aged 68, was first seen May 7, 1947, complaining of an eruption of eight days' duration He had not been vaccinated but had been shaved by a barber twice weekly prior to the appearance of the eruption It was not determined whether the barber had been vaccinated or whether he had had recent contacts which might have resulted in the vaccination of the patient An adult son had been vaccinated but lived separately from the father, and little or no contact had occurred between them preceding the infection The probability is strong that the vaccination occurred in the barber shop

The patient's appearance was striking, as all lesions were located in the bearded area There were at least thirteen lesions, but several on the right side of the chin had become confluent, so that there was now one huge, inflamed and necrotic mass Most of the other lesions had remained discrete and were present on the left side of the chin and on both cheeks All had the appearance of strong vaccination "takes," and consisted of inflamed bases with pustular and necrotic centers Some were slightly crusted Healing was uneventful, and most of the lesions, including even the large confluent one, had disappeared completely in ten to fourteen days Deep scarring marks the site of the confluent area, but the remaining lesions have left only superficial redness, which may disappear entirely

DISCUSSION

DR HOWARD FOX I think that it is possible that the patient acquired the vaccinia in the barber shop A number of years ago I was lecturing at New York University on eczema and mentioned that one of the dangerous sequelae was vaccinia, saying that no child with eczema should be vaccinated While lecturing I got a note from the pediatric department asking me to come to Bellevue Hospital to see a child The child was a 2 year old Negro with typical lesions of vaccinia on a large part of the body, which he had contracted from an older sister who had recently been vaccinated He died in about six days

DR ANTHONY C CIPOLLARO The thought came to me that these sequelae might be prevented by covering vaccinations Patients rub and scratch and reinoculate, and for this reason I have covered vaccinations in members of my family and in my own case I think that it prevents this sort of accidental vaccinia

DR EUGENE F TRAUB I thought that I had fairly well excluded all sources of inoculation but the barber shop The only other member of the family who had been vaccinated was an adult son, who did not use the same bathroom as his father

Sarcoidosis in a Negro Woman Aged 33 Years Presented by DR. A BENSON CANNON

DR HIRAM E MILLER In general, I believe that these patients will be seen by the psychiatrist for a visit or two, and then they will come back to the dermatologist If their delusions are well established, little can be done for them by the psychiatrist or the dermatologist

DR E J RINGROSE (by invitation) Favorable results have been achieved with patients with dermatitis factitia who would submit themselves to interview Most of the patients, under the influence of sodium amytal® (sodium isoamylethylbarbiturate) given intravenously, will admit what they have been using

DR MERLIN T-R MAYNARD, San Jose, Calif One of the patients admitted the use of needles and pincers Her euphoric personality fits into the diagnosis readily The other one started talking about herself and her troubles immediately, which fits into the picture of a neurosis of the neurotic excoriation type, a typical picture Nodules particularly can be produced by a traumatic agent We all see children pick and squeeze their skin, but it does not result in hemorrhage into the areas

DR ERVIN EPSTEIN I realize that the condition in such cases is usually diagnosed as dermatitis factitia, and I am willing to accept that diagnosis for these patients However, I am unable to see how the primary subcutaneous nodules could be produced mechanically

A Case for Diagnosis (Bacteremia?) Presented by DR FRANCES A TORREY

A Case for Diagnosis (Dermatitis Medicamentosa?) (Purpura Annularis Telangiectodes?) Presented by DR FRANCES M KEDDIE

V D C, a 47 year old Portuguese woman, was first seen in the University of California Dermatology Clinic in March 1945, at which time a diagnosis of black hairy tongue was made No cutaneous eruption was present at that time

On April 1, 1946, she returned to the clinic because of lesions of both legs of about ten months' duration There are numerous pigmented purpuric macules of various sizes and shapes Many of these lesions show telangiectasia The patient states that she had taken "sleeping pills" regularly for many years The physical examination revealed no abnormalities

Laboratory examination revealed 4,400,000 erythrocytes, 90 per cent hemoglobin and 8,900 leukocytes, the differential count was normal The sedimentation rate was 11 mm in 1 hour The capillary clotting time was 8 minutes The tourniquet test at a pressure of 80 mm of mercury for 15 minutes caused numerous petechiae The prothrombin time was 80 per cent The urine was normal

Microscopic sections showed increased deposition of pigment in the basal cell layer and occasional deposits of hemosiderin in the cutis Extravasation of red blood cells and hyalinization of several vessel walls were noted A perivascular infiltrate consisting of lymphocytes and polymorphonuclear leukocytes was present

DISCUSSION

DR NORMAN EPSTEIN This case suggests Majocchi's disease

DR STUART WAY A diagnosis of dermatitis medicamentosa is in order, but not Majocchi's disease This case has none of the characteristics of purpura annularis telangiectodes in the cases that I have reported

DR HIRAM E MILLER This is a good example of purpura, but not of purpura annularis telangiectodes There is no definite annular appearance, and there are no telangiectases It may be a toxic purpura, but not Majocchi's disease

A Case for Diagnosis (Lichen Planus? Lupus Erythematosus?) Presented by Dr Maurice J Costello

Hereditary Hemorrhagic Telangiectasia with Hemangioma Presented by Dr John N Graham

A Case for Diagnosis (Lichen Planus Hypertrophicus? Amyloidosis?) Presented by Dr Anthony C Cipollaro

Psoriasis Exacerbation Following Vaccination Presented by Dr George M Lewis

B O, a woman aged 23 from New York Hospital, has had psoriasis since the age of 6, limited to the elbows, scalp and sacral region, with mild exacerbations and remissions Five weeks ago she was vaccinated, and three days later numerous small psoriasiform lesions developed on the trunk, face, neck and extremities A confluent nummular patch of psoriasiform lesions appeared at the vaccination site, and the long-standing patches on the elbows and scalp became larger One sister also has psoriasis

There are numerous dime-sized to quarter-sized erythematous scales distributed over the face, neck, trunk and extremities The vaccination area shows a dollar-sized psoriasiform patch The Mazzini reaction of the blood was negative The results of biopsy were compatible with acute psoriasis

DISCUSSION

Dr George M Lewis This is the third patient we have seen with an acute attack of psoriasis developing immediately after vaccination Since the cause of psoriasis is not known, one could consider that in some way the virus infection had had a specific effect on the disease

Lichenoid Miliary Sarcoid Presented by Dr Maurice J Costello

A Case for Diagnosis (Pemphigus?) Presented by Dr A Benson Cannon

Vaccinia, Generalized, Following Vaccination for Smallpox Presented by Dr A Benson Cannon

Leprosy, Lepromatous Type, with Tufted Destruction of the Tips of the Terminal Phalanges Presented by Dr Maurice J Costello

B O, a man aged 20, a Puerto Rican, is presented from Willard Parker Hospital, to which he was transferred from Harlem Hospital He had sought attention at the latter institution on March 13, 1947, because of pain in the right groin, severe nausea and vomiting Intestinal obstruction was considered on admission, but the gastrointestinal symptoms subsided with conservative treatment

While the patient was in Harlem Hospital, a cutaneous eruption was noted, although his skin was reported to have been clear on admission He had noted scaling of the feet in October 1946 No one in the family has a similar eruption and there has been no known contact with leprosy The patient has been in the United States for about eight months

DR FRANCES M KEDDIE When the patient was first seen the lesions were annular and telangiectatic, now they are purpuric and diffuse Tonight she stated that she had been taking "sleeping pills" for one year only This eruption is certainly of not more than one year's duration and may be a toxic reaction to self medication

Dissecting Cellulitis of the Scalp (Perifolliculitis Capitis Abscedens et Suffodiens) Presented by DR GRANT MORROW

A Case for Diagnosis (Psoriasiform Eruption? Lymphoblastoma?) Presented by DR FRANCES A TORREY

A Case for Diagnosis (Keratosis Palmaris et Plantaris Associated with Carotenemia? Pityriasis Rubra Pilaris?) Presented by DR H V ALLINGTON

Hodgkin's Disease and Cutaneous Torulosis Presented by DR FRANCES A TORREY (previously presented by DR TORREY at the April 1945 and October 1945 meetings of the San Francisco Dermatological Society)

A Case for Diagnosis (Localized Scleroderma?) Presented by DR NORMAN EPSTEIN and DR. JULES KEY (by invitation)

A Case for Diagnosis (Melanosis of Riehl?) Presented by DR H V ALLINGTON

V G, a white woman aged 46, was seen first on April 11, 1946 She presented a brownish pigmentation of the face, the neck, the exposed portion of the upper part of the chest and to a lesser degree of the arms The skin also showed irregular telangiectasia and erythema and on the cheeks was shiny and glazed The patient stated that this condition had been present a little over two years

The patient attributed this to exposure to the fumes from hot lubricating oils in her work for an oil company Her work consisted in running viscosity tests and gaging tanks of hot oil She had done this work for about four years She stated that exposure to the fumes from the hot oil caused her skin to burn and sting and become "purplish pink" After work, cool applications were required to quiet the burning sensation Recently she used vinegar for relief She had not done anything previously about her problem because she was anxious to hold her job, which she liked She had also noticed that exposure to sunlight caused increased redness, burning and stinging However, her work was indoors, and exposure to light was kept at a minimum She further stated that exposure to the fumes of heavy oils was more irritating than to that of light oils

She is for the most part a vegetarian She does not eat carrots or other carotene-containing foods to excess, however, and the character of her pigmentation is not that of carotenemia

I believe that this patient is one who is sensitive to the fumes from hot oils and that her reaction is primarily on this basis An endocrine or dietary deficiency may be present and may increase the sensitivity of her skin

DISCUSSION

DR HARRY J TEMPLETON I saw this patient with Dr Allington, and at that time there was a question of industrial liability The patient has some

Biopsy at Harlem Hospital showed cutaneous nodular leprosy

Roentgen examinations at Willard Parker Hospital showed destruction of the tufted ends of all terminal phalanges of the fingers and toes There was periostitis of the proximal phalanges of all four fingers of the right hand

Results of roentgenographic examination of the chest were normal, ruling out sarcoid The Kline reaction of the blood was 4 plus, and the Mazzini reaction was negative Determinations of the chemical content of the blood showed a reversal of the albumin-globulin ratio, the albumin being 2 Gm and the globulin 6 Gm A blood cell count revealed 4,260,000 red blood cells and 11,500 white blood cells, with 65 per cent polymorphonuclear leukocytes, 24 per cent lymphocytes, 7 per cent eosinophils and 3 per cent large mononuclear cells The urine was repeatedly normal A nasal smear showed lepra bacilli

DISCUSSION

DR HOWARD FOX The man who made the original diagnosis, probably Dr Irgang at Harlem Hospital, is entitled to much credit The patient comes from a country where leprosy is endemic, but one must examine him carefully to discover any changes The ulnar nerves are unquestionably enlarged all the way to the axillas, and one may press on them hard without causing any pain, which is much in favor of leprosy There are nodules on the ear and some enlargement of the great auricular nerve, although there is no anesthesia In a recent article Arnold expressed the belief that examination of the nasal smear for lepra bacilli is of little diagnostic help It is not the best way to prove a diagnosis of leprosy The radiologic changes in the phalanges in this case are significant

George M Lewis, M D, *President*

John C Graham, M D, *Secretary*

Nov 25, 1947

Lichen Planus Limited to the Oral Mucosa Presented by DR GEORGE M LEWIS

E S, an American lawyer aged 43, discovered an asymptomatic white lesion on his tongue eleven months ago Six months later he saw his physician and then an oncologist, both of whom made a diagnosis of leukoplakia

The patient smoked two pipes and fifteen cigarets daily, used magnesia magma as a mouthwash and a magnesia magma tooth paste He took a "vitamin pill" daily and a "sleeping pill" every two weeks In June 1947, when I first saw him, there was a bluish white lesion on the dorsum of the tongue about 2 by 1 cm in extent, an area similar in appearance was present inside the cheek opposite the lower right molars A circinate lesion was found near the oral commissure on the buccal mucosa of the left cheek

The patient has not smoked since June He is using a bland mouthwash Partial involution of the lingual lesion has occurred, but those on the buccal mucosa have remained unchanged

DISCUSSION

DR HOWARD FOX It is sometimes difficult to differentiate between leukoplakia and lichen planus, but as Dr Combes said, leukoplakia tends to be thickened and rough and even verrucous, which lichen planus does not Without biopsy, it is difficult to tell in some cases I think that this patient probably has lichen planus

sort of poikiloderma I do not know whether it is melanosis of Riehl or poikiloderma of Civatte or whether it is primarily an abnormal reaction to light and to tar and oil I think that Dr Fasal is able to tell us more about melanosis of Riehl since he worked in the Riehl clinic, with both the elder and the younger Riehl

DR PAUL FASAL I think that this is a case of melanosis, but not melanosis of Riehl Riehl included in his description only cases due to ingestion of toxic products Those cases were seen after World War I when people used various food substitutes containing toxic products I consider this disease a tar melanosis, but not melanosis of Riehl

DR F G NOVY JR In a generalized Berloque dermatitis there is the same problem of perfumes plus sunlight This woman is probably a sensitive person who has been exposed to various tar products and sunlight and has reacted with the formation of pigment

DR HIRAM E MILLER I agree with Dr Fasal It is melanosis, but not melanosis of Riehl or poikiloderma Dr Templeton made the statement that he thought it was melanosis of Riehl or poikiloderma and that there was a question of industrial liability I believe that if either of these two diagnoses were accepted, there would be no question about industrial responsibility The distribution of lesions here is not that of melanosis of Riehl, because, as I understand it, the scalp is always involved in this disease In this patient the scalp is not involved The patient has no involvement around the breasts and in the axillary folds as is usually observed Melanosis of Riehl is of toxic origin, while in this patient the causative factor is tar and oil plus sunlight For these reasons I believe that it is melanosis, but not melanosis of Riehl

DR HARRY J TEMPLETON I agree with Dr Novy that this is due to action of tar or oil on skin which has become sensitized to sunlight

DR REES B REES According to the textbooks, in tar melanosis the distribution is confined to face, scalp, shin, hands and forearms There is pigmentation, but telangiectasia or atrophy is not mentioned The patient has telangiectasia

DR MERLIN T-R MAYNARD, San Jose, Calif The fact that the patient is a machine operator should be considered Hot tars and oils become volatile Considering the fact that tar could have been ingested through three channels, the skin, the respiratory tract or the mouth, it is possible that she has ingested a certain amount of it through the respiratory system The traps of respirators demonstrate that one eats what one breathes This could therefore be melanosis of Riehl in the classic sense

ERVIN EPSTEIN, M D, *President*
FRANCES M KEDDIE, M D, *Secretary-Treasurer*
Sept 13, 1946

Pemphigus of the Conjunctiva Arsenical Pigmentation and Keratoses from Fowler's Solution. Presented by DR OTTO E L SCHMIDT

Angiokeratoma? Presented by DR OTTO E L SCHMIDT

Subcutaneous Granuloma Annulare Presented by DR HIRAM E MILLER

T H S, a four year old white boy, was first seen in the University of California Hospital on July 9, 1946, with a chief complaint of multiple nodules

DR ANTHONY C CIPOLLARO I agree with the presenting diagnosis I think that too often patients with leukoplakia are given a serious prognosis Carcinoma does develop in patches of leukoplakia, but it is of rather infrequent occurrence, and people interested in the cancer problem lead us to believe there must be a definite sequence from leukoplakia into cancer, which *I think is erroneous* I recently saw a physician with extensive lichen planus all over the body, with extensive lesions on the buccal mucosa, including the border of the lip, and on the vocal cords, causing him to be hoarse They could be seen distinctly with the laryngeal mirror I have never seen or read of lesions of lichen planus on the vocal cords

DR GEORGE C ANDREWS I think that fear of leukoplakia is well warranted by the fact that often when it does become cancerous the lesion is extremely serious and by the fact that one never knows in a case of leukoplakia whether cancer cells are present or not One may take a biopsy specimen from one portion of the leukoplakia and histologically find only leukoplakia and then cut some more sections and find cancer So it is a serious disease, and I believe that lichen planus of the mouth is also a serious disease, especially if it lasts over some time I have had 2 patients with lichen planus of the buccal mucosa in whom cancer of the buccal mucosa developed after the lesions had been present for twenty years It is certainly a precancerous disease I do not think that the fact that this man has lichen planus means that he has nothing to worry about The patient should be treated and should be watched, told to stop smoking and given vitamin B complex and whatever other therapy may be available

DR JOHN C GRAHAM I agree with the diagnosis It seems to me that the lesion on the tongue was rather typical of a healing lichen planus

DR HOWARD FOX I had occasion to write up a series of 10 cases of lichen planus confined to the mouth One of the patients, a man whom Dr Udo Wile had seen, was a great smoker and for eight years had had attacks of lichen planus that flared up after smoking, when he stopped smoking the eruption quieted down

DR GEORGE M LEWIS I believe, as Dr Andrews does, that a patient with lichen planus of the buccal mucosa should stop smoking, and the patient was so advised He was given a bland mouthwash but no other treatment because my results have been rather poor in treating lichen planus of the buccal mucosa

Edema Due to Hypoproteinemia Presented by DR FRANK C COMBES

D E, a white girl aged 16, was admitted to Bellevue Hospital complaining of long-standing swelling of both legs It was noted a few days after birth, but it was not known whether it was confined to the legs The patient states that the swelling disappeared spontaneously from the age of 2 years until she was 8 When at the age of 9 or 10 years the swelling recurred, she entered Mount Sinai Hospital, where extensive studies were done and reported (Schick, B, and Greenbaum, J W Edema with Hypoproteinemia Due to Congenital Defect in Protein Formation [Case Report], *J Pediat* **27** 241-245 [Sept] 1945) After her discharge the swelling of the legs remained stationary with no accompanying fever, inflammation or tenderness In 1946 she reentered Mount Sinai Hospital twice, blood plasma transfusions were given with but temporary relief, the swelling would go down for two days and then recur Her most recent admission to Mount Sinai Hospital took place in the summer of 1947 At that time, in addition to the usual swelling of the extremities, there was edema of the face, back and abdomen She was treated with sodium and potassium acetate, as a result of which the condition of all but the legs returned to normal The edema of the legs has persisted

on the legs and back of the head of about eight months' duration A history of a fall prior to their appearance was obtained, but subsequently more nodules developed without preceding trauma

Positive physical observations include nontender firm fixed nodules on the left occipital region, larger purplish nodules on the right tibia and similar smaller nodules on the left knee There is generalized nontender moderate adenopathy Routine tests revealed that the blood and urine were normal The reaction to an intracutaneous tuberculin test, in dilution of 1 1,000, was negative The reaction to the coccidioidin test, in dilution of 1 1,000, was negative The blood cholesterol was 112 mg per hundred cubic centimeters Serum protein was 6 mg per hundred cubic centimeters (albumin 3 8 Gm and globulin 2 2 Gm) Serum calcium was 12 mg and serum phosphorus 4 48 mg per hundred cubic centimeters Phosphatase was 6 2 Bodansky units Roentgenograms of the chest and long bones showed no abnormalities Biopsy of the marrow revealed a normal differential count Microscopically the sections of a nodule showed a focus of coagulation necrosis of the connective tissue surrounded by radiating strands of fibroblasts, epithelioid cells and lymphocytes in palisade arrangement (Starting Aug 20, 1946, both cutaneous lesions were irradiated, a total of 200 roentgen rays was used with a 3 mm filtration of aluminum)

DISCUSSION

DR REES B REES I saw this patient on the ward with Dr Miller, Dr Keddie and other members of the staff At that time we thought of sarcoid, having just the clinical appearance to go on The lesion on the left knee was clinically suggestive of granuloma annulare, but we did not think of that diagnosis until the histologic section was studied Dr Brown found an interesting article by Udo Wile on this subject

DR MARSHALL BROWN (by invitation) This article appeared in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY (**30** 785, 1934), a report of an unusual case of granuloma annulare by Dr F G Graver and Dr Udo Wile, of the University of Michigan Medical School The first reports were in 1908 by a British writer, Dr Graham Little He reported several cases of possible subcutaneous granuloma annulare The next reports were written in 1931 by Jacobi (Jadassohn, J Handbuch der Haut- u Geschlectskrankheiten, Berlin, Julius Springer, 1931, vol 10, p 796) He reported several cases of subcutaneous granuloma annulare which occurred on the palms and the flexor surfaces of the fingers, and the dorsal surfaces of the feet and lower extremities However, there were no case reports at that time of subcutaneous granuloma annulare occurring in the scalp The case reported by Dr Wile occurred in a 2 year old white boy who was admitted to the hospital with a history of subcutaneous nodules on the scalp, the flexor surface of the left wrist and the extensor surface of the right tibia Our patient's mother stated that the first time she noted nodules on the flexor surface of the wrist was five months prior to the patient's entrance into the hospital Three months before admission she noted five nodules occurring in the subcutaneous tissues of the scalp, and two months before admission she noted nodules occurring on the extensor surface of the right tibia Physical examination revealed subcutaneous nodules which were firm and attached to the underlying tissue, and the overlying skin was loose and movable There was no previous history of tuberculosis Members of the family were examined for tuberculosis, no evidence of this disease was found In the hospital the patient was asymptomatic

DR E K STRATTON Have a tuberculin test and guinea pig inoculation been done?

unchanged up to the present On elevation of the feet, the edema shifts to the thighs and abdomen Hematologic studies at Mount Sinai Hospital showed essentially normal conditions except for hypoproteinemia The report of protein fractionation revealed reduction of all protein fractions, with complete absence of gamma globulin

Studies at Bellevue Hospital showed a total protein content of 5 2 Gm with albumin 2 6 Gm and globulin 2 6 Gm The cephalin-cholesterol flocculation reaction was negative On another occasion the total protein was 4 5 Gm (albumin 3 3 Gm and globulin 1 2 Gm)

Examination shows both thighs and legs to be indurated with a noninflammatory type of edema which pits on deep pressure The enlargement of the left is the greater of the two The skin of both legs shows slight thickening, with a little pigmentation and a few nodular infiltrations There appear to be constricting bands around the ankles There is slight pitting edema of the dorsa of both hands The face, especially around the malar bones, seems slightly puffy Some reduction of the swelling of the legs is noted on elevation

DISCUSSION

DR GEORGE C ANDREWS I am pleased to have seen this case because I have a patient with similar swelling of the legs of unexplained cause, but a study of the serum proteins has never been made It is interesting to me that this condition of the serum globulin exists I did not realize that people live without gamma globulin What was the interval in dates between the globulin determinations?

DR GERALD F MACHACEK Dr Combes noted a discrepancy in the determinations in different institutions

DR MAURICE J COSTELLO If one did not know the history of absence of serum globulin, one would almost think this patient had Milroy's disease She has lymphangiectases and fibrous nodules on the anterior tibial regions She had her first attack of erysipelas of the leg while she was in the hospital She has been quite free of infections of all types, I asked her whether she had ever had measles, and some one said her brother had the disease but the patient was given gamma globulin in the incubation stage and acquired measles in a mild form

DR GEORGE M LEWIS Will Dr Combes please outline the difference between this condition and Milroy's disease?

DR MAURICE J COSTELLO Apparently this patient's symptoms have remained exactly the same through the years, so one would not expect much change in the globulin estimations You will recall a case that I presented last year for Dr Wise, that of the baby of a physician who presented an unusual generalized edema not unlike that shown by this patient I shall advise the father regarding this case and suggest determinations of the gamma globulin

Sclerodactylia (?) Following Myocardial Infarction Presented by DR GERALD F MACHACEK

DISCUSSION

DR GERALD F MACHACEK I ran across an article by A H C Johnson in the *Annals of Medicine* (**19** 433-456, 1943) reporting a series of 178 consecutive cases of myocardial infarction, in 21 8 per cent of which the patient evidently presented this type of lesion In the same volume Kenneth C Kehl (pp 213-223) reported 6 cases of Dupuytren's contracture in the presence of myocardial infarction

DR REES B REES A guinea pig inoculation was done at the Permanente Hospital, but the result was not reported to us Necrobiosis lipoidica diabeticorum resembles this disease histologically, but the comparison ends there

A Case for Diagnosis (Actinic Dermatitis? Lupus Erythematosus?) Presented by DR REES B REES

Carotenemia Presented by DR H V ALLINGTON

A Case for Diagnosis (Monilethrix?) Presented by DR H V ALLINGTON

Generalized Progressive Scleroderma Presented by DR WILLARD M MEININGER

A Case for Diagnosis (Progeria? Lupus Erythematosus?) Presented by DR FRANCES M KEDDIE

D A B, a 6 year old white girl, was first seen in the University of California Dermatology Clinic on Aug 12, 1946 Dermatitis has been present on the face since the age of 6 months One year ago she sustained second degree burns of her arms and back which required skin grafting In the pediatric clinic a diagnosis of microcephaly, dwarfism and congenital heart disease was made

At the present time there is a rather diffuse blotchy erythematous scaly eruption with scarring and atrophy involving the nose and cheeks There are numerous, discrete, erythematous, papular and excoriated lesions on the extremities The lids are reddened and crusted and the conjunctivas injected Her height, weight and skeletal measurements are below normal for her age

There were no abnormal observations in laboratory studies of the blood, urine, glucose tolerance and urine porphyrins The tuberculin cutaneous reaction was negative

DISCUSSION

DR HARRY J TEMPLETON I presented the same patient with the same diagnosis at one of our previous meetings My co-workers and I have studied this case at the Children's Hospital in Oakland and wound up just where we started Not only was there some abnormal delay in the general development of the child, but of the skull, the heart and the child's skin, and for lack of a better classification it was called progeria I cannot say that the lesions have made much progress or retrogression, they are still in status quo The child is not microcephalic, she is rather bright for her age

DR W F HARDING (by invitation) We do not feel that this disease quite fits into the picture of progeria The child does not show atrophic changes in the skin She has no loss or graying of hair or arteriosclerosis Talbot of Harvard has studied a number of cases of progeria The results of all metabolic studies made in these cases were within relatively normal limits Talbot and his co-workers came to the conclusion that in cases studied the caloric intake and output was more or less in equilibrium, all the heat and energy being expended without anything being left over for body development Most patients showed greatly increased metabolism without hyperthyroidism

This patient seems to be acquiring that condition as well It could be explained on the basis of anoxemia Going into the possibility of whether the condition was due to the coronary sclerosis, Johnson came to the conclusion that it probably is a cardiac pain reflex because of the peculiar connection between the first thoracic segment and the lower cervical and upper thoracic sympathetic ganglions, causing reflex constriction of the vessels of the hands "Trophic" ulcers of the hands following coronary disease also occur

A Case for Diagnosis (Bullous Lupus Erythematosus?) Presented by DR MAURICE J COSTELLO

A Case for Diagnosis (Dermatitis Medicamentosa? Mycosis Fungoides?). Presented by DR HOWARD FOX

Epidermal Cyst on the Finger Presented by DR MAURICE J COSTELLO

Dermatitis Herpetiformis and Lupus Erythematosus Occurring Consecutively and Simultaneously in a Patient Who Had Had Splenectomy for Purpura Hemorrhagica Presented by DR MAURICE J COSTELLO

George M Lewis, M D, *President*
John C Graham, M D, *Secretary*
Dec 16, 1947

Acnitis Presented by DR A BENSON CANNON

A Case for Diagnosis (Ulcus Vulvae Acutum? Triple Symptom Complex of Behcet?) Presented by DR A BENSON CANNON

Chronic Lymphedema of the Face, Hypertrophic Gingivitis, Rosacea Presented by DR ANTHONY C CIPOLLARO

A S, a woman aged 45, first noticed swelling of the upper lip, nose and right side of the face eleven years ago, with less involvement of the left side of the face These episodes of swelling were thought to be due to some infection of the teeth, but multiple extractions yielded no improvement The patient suffered an attack of Bell's palsy on the right side about ten years ago, accompanied with a severe exacerbation of the facial swelling on the affected side, and this has continued more or less unabated up to the present The condition is greatly aggravated by exposure to cold or dampness

The patient presents a nonpitting, moderately firm, edematous swelling of the cheeks, nose and right periorbital tissues The right side of the face shows the greater involvement In addition, there is a papular eruption of the nose and cheeks with moderate erythema of the affected areas The gingivae are greatly swollen

DISCUSSION

DR RAY H RULISON I have never seen that type of gingivitis The patient said that her dentist had taken roentgenograms of those teeth and found them perfectly sound I thought that the swelling of the gum was related to the lymphedema

Adenoma Sebaceum Multiple Sebaceous Cysts with Hypertrophy and Hyperplasia of Sebaceous Glands Presented by DR JOHN M GRAVES

A Case for Diagnosis (Pemphigus Vegetans?) Presented by LIEUTENANT COLONEL ROBERT S HIGDON, Medical Corps United States Army, Letterman General Hospital, San Francisco (by invitation)

J R, aged 34, while stationed in Tokyo, noticed slight intermittent epistaxis on April 15, 1946 Examination revealed a pinhead-sized creamy white papule ½ inch (1 27 cm) within the right nares on the lateral wall The papule grew rapidly and, within one week, had reached the size of a bean and was verrucous in appearance Within two weeks continued growth caused partial obstruction of the right nares At this time a second whitish pinhead-sized papule was noted just inside the left nares on the medial wall He was given treatment with sulfonamide drugs By the third week, the right nares was completely occluded and the second lesion had grown so rapidly that the left nares was partially occluded He was admitted to the 42d General Hospital in Tokyo, on May 6 Treatment with sulfonamide drugs was discontinued The verrucous growths were removed from both nares with electric cautery Within a week the lesions reappeared, accompanied with signs of secondary infection Results of dark field examination, biopsy, smears, cultures and serologic and blood tests were negative The lesions rapidly regenerated, completely obstructing both nares, and extended externally to involve all surfaces of the lower portion of the nose for a distance of 1 cm The patient was given one hundred and nine intramuscular injections of penicillin (40,000 units each) for a total of 4,360,000 units While he was receiving penicillin, three new papules developed, one on the central portion of the upper lip and one on each lateral aspect of the chin These papules grew rapidly until they reached a diameter of 2 cm, were verrucous in appearance and exuded a clear serous fluid All laboratory work (including biopsy) was repeated, but results were again negative The patient was evacuated to the United States by plane and admitted to Letterman General Hospital on July 26 Smears, cultures, animal inoculation, biopsy, serologic and blood examinations, urinalysis and roentgenograms of the chest have revealed no abnormalities The lesions continued to spread and have gradually involved the entire chin, lower lip and midportion of the upper lip Three weeks ago the mucosa over the soft palate, uvula, pharynx and tonsillar areas became erythematous, causing some pain on deglutition Topical applications have consisted of boric acid, benzalkonium chloride and penicillin and bichloride of mercury compresses Penicillin in oil (300,000 units) was given intramuscularly daily for ten days Two intravenous injections of oxophenarsine hydrochloride were administered Nitrofurazone was applied to the lesions for twenty-six days None of these medications was of benefit Fractional dosage of low voltage roentgen therapy has seemed to retard further extension of the lesions but has not caused involution

DISCUSSION

DR HARRY E ALDERSON The patient stated that his trouble started in the nose His nostrils are completely occluded Unfortunately, I was not able to examine his palate My former associate, Dr Esteban Reyes, of San Salvadore, has sent me many photographs of cases of rhinoscleroma, some showing extensive vegetation on the outer part of the nose On the external part of the nose there were verrucous growths not ordinarily associated with rhinoscleroma There could

DR HOWARD FOX At first glance this swelling looked like a paraffinoma It is a lymphedema of unknown origin, and I do not believe that anything can be done for it

DR MAURICE J COSTELLO I think that this patient should be studied thoroughly A focus of infection may be found in the sinuses During the course of the examination there was a constant seropurulent discharge from the nose, and I think temporary improvement might be obtained by the administration of sulfonamides, especially sulfathiazole I suggest a trial of streptomycin

DR A BENSON CANNON The lesions in this case remind me more of granuloma inguinale than any other condition that I am acquainted with, and I should investigate the case with that diagnosis in view I should also perform a Frei test and have a hematologist study her leukocytes and, perhaps, take a bone marrow specimen

DR GEORGE C ANDREWS I suspect a diagnosis of solid edema of the face I was also thinking of leukemia because some of the infiltration suggests that diagnosis, and hypertrophic gingivitis may occur in leukemia

Tinea Capitis (Microsporum Lanosum) in Mother and Son Presented by DR ANTHONY C CIPOLLARO

Syphilis (or Tuberculosis Cutis of a Buttock?) Presented by DR GEORGE C ANDREWS

Balanitis Xerotica Obliterans Presented by DR A BENSON CANNON

N T, a man aged 37, first consulted me on June 14, 1947, complaining of phimosis and preputial fissuring, which began fourteen months previously The lesions began with small erosions or fissures on the frenulum praeputii penis which occasioned slight stinging on micturition Healing of the erosions was followed by the development of a grayish white, scarlike process which gradually increased to form a band about the prepuce Retraction of the prepuce has become increasingly difficult, and its performance causes fissures to appear

Examination shows a compact, well built man whose blood pressure is 128 systolic and 90 diastolic He has a fairly well advanced temporal thinning of the hair The prepuce is long and presents numerous superficial radial fissures There is a dense bandlike thickening about the circumference of the prepuce extending to the frenulum praeputii penis and the urinary meatus The thickened areas have a dull, gray-white appearance The urinary meatus seems narrowed Much smegma is present in the preputial sac

The basal metabolic rate was —11 2 per cent The Mazzini reaction of the blood was negative on two occasions The blood arsenic level was 0 32 mg per 10 Gm of dried blood

With the use of a simple protective paste the fissure of the prepuce healed promptly and retraction ceased to be painful though the cicatricial changes persisted In August 1947 treatment with vitamin E (eprolin–S®) was begun in doses of 5 Gm three times daily Despite this, the tightness of the prepuce increased, and by October retraction could be accomplished only with the assistance of soaping and considerable traction On October 28 treatment with tripelennamine hydrochloride (pyribenzamine hydrochloride®) was begun with 200 mg daily, increasing to 400 mg a day Use of vitamin E was also continued After three weeks on this regimen the patient felt that he had initially shown some improvement but that the process was stationary at that time

be a superimposed infection of some sort I think that it would be worth while to look for Frisch bacilli I could not find any record of such examinations having been made here The patient is apparently in good general health, despite the extensive lesions on his nose

DR PAUL FASAL This case reminds me of 2 cases of rhinosporidiosis which I have seen I would suggest the use of antimony potassium tartrate as a therapeutic experiment

DR HARRY J TEMPLETON I thought that it was a typical vegetative lesion of bromide or iodide dermatitis

DR JAMES DRAKE While in Japan, this soldier drank almost entirely from Lister bags The possibility of the unauthorized use of an iodide as a water purifier occurs to me Has the question of iodide ingestion been investigated?

DR E K STRATTON If this eruption were in the groin I would think of granuloma inguinale I have seen cases of this disease in the groin with subepidermal pustules as well as the granulomatous lesions similar to what this case presents I agree with Dr Fasal that antimony therapy should be tried

LIEUTENANT COLONEL ROBERT S HIGDON (by invitation) Rhinoscleroma was suspected, and I have tried to demonstrate the causative agent of that disease by smears, cultures and biopsy sections, but have been completely unsuccessful thus far Bromides and iodides were also considered, and the patient was given tests accordingly, but these tests have also been without positive results

Thymoma Presented by DR FRANCES A TORREY

Ervin Epstein, M D, *President*

Frances M Keddie, M D, *Secretary-Treasurer*

Nov 15, 1946

Balanitis Xerotica Obliterans Presented by DR E A LEVIN

A Case for Diagnosis (Behcet's Syndrome? Pemphigus?) Presented by DR JOHN M GRAVES

Multiple Neuromas of the Skin Presented by DR ERVIN EPSTEIN

J W, a 24 year old white man, presents a nodular eruption below the right lower lid, on the lid and on the margin The lesions consist of shiny, smooth, flesh-colored discrete and coalescing nodules They are firm Some of the older lesions show hyperkeratosis of the surface, possibly due to previous therapy

The disease started ten years ago, after an injury The patient stated that when he arrived home some "goose pimples" were present below his right eye and that these have enlarged and slowly spread during the past ten years The lesions are asymptomatic

Treatment has included "freezing," one year ago, "burning with an electric needle," one month later, and the use of "acid" by the patient on numerous occasions since This has failed to eradicate the lesions or to stop the development of new ones

DISCUSSION

DR EUGENE F TRAUB Dr Cannon gave this patient pyribenzamine,® and to the best of my knowledge it has not been used in this disease before, although patients with scleroderma show considerable benefit from its use Certainly Dr Cannon has helped this patient and that is to be remembered, as it is the first drug that has influenced this disease, as far as I know

DR HOWARD FOX I suggest circumcision and think that it would relieve the whole trouble The little band is in the foreskin

DR A BENSON CANNON I am under the impression that a number of cases have been reported in which this condition is said to have followed circumcision and that one should avoid that operation, if possible, under these conditions This patient had symptoms suggestive of endocrine disturbance, such as sweating of the palms, rapid pulse and other emotional disturbances and a basal metabolic rate of —12 per cent It was because of these symptoms that we prescribed diphenhydramine (benadryl®) He had had large doses of vitamin E uninterruptedly for four months without any change in his condition

A Case for Diagnosis (Carcinoma of the Mouth? Gumma of the Mouth?) Presented by DR ANTHONY C CIPOLLARO

A Case for Diagnosis (Sarcoid?) Presented by DR GEORGE M LEWIS

A Case for Diagnosis (Sarcoid? Syphilis) Presented by DR MAURICE J COSTELLO

Syringoma Presented by DR GEORGE M LEWIS

A biopsy section studied by Dr Gerson R Biskind revealed neuroma The sections showed a loose fibrous stroma covered on one aspect by a thin layer of skin In the stroma were several sharply demarcated bundles of cellular tissue that had a limiting membrane of fibrous tissue The cells had a slender almost wavy nucleus The stroma around the cells was pink and homogeneous but in places might be fibrillar The cells did not show distinct palisading with the formation of characteristic Verocay bodies, this process, however, was suggested in many places The over-all pattern was highly suggestive of an amputation neuroma, except that the bundles were much more cellular The site of excision should be observed for possible recurrence The present histologic structure showed no evidence of malignancy

DISCUSSION

DR HIRAM E MILLER I am not familiar with neuromas that are not painful In my patients, all of them were painful Kyrle, however (quoted in the textbook by Ormsby and Montgomery), described painless tumors in the retroauricular region in a patient who had neuromas for three years They were lentil-sized, translucent areas Histologically the lesions consisted of bundles of delicate nerve fibers He stated that pain was absent because they were "unripe" neuromas The lesions in this case may be of a similar nature

DR ERVIN EPSTEIN This disease is apparently rare It usually follows trauma The lesions seem to resemble amputation neuromas histologically They are usually painful, but some do exist for long periods before pain develops According to the literature, all become painful eventually Plastic surgery followed by skin graft would seem to be the treatment of choice in this case

Lichen Sclerosus et Atrophicans, Inframammary, Inguinal and Vulvar Presented by DR ERVIN EPSTEIN

Lupus Erythematosus Presented by DR NORMAN N EPSTEIN

Calcinosis Cutis (Circumscribed Form) Presented by DR HIRAM E MILLER

A Case for Diagnosis (Actinic Dermatitis? Lupus Erythematosus?) Presented by DR REES B REES

A Case for Diagnosis (Actinic Dermatitis?) Presented by DR FRANCES A TORREY

Bowen's Disease? Presented by DR GRANT MORROW

Scleroderma (Localized) Presented by DR ROBERT A STEWART

Nevoxanthoma-Endothelioma Presented by DR MAX KRAUSE

A Case for Diagnosis (Scaly Erythroderma? Lymphoblastoma?) Presented by DR EDWARD A LEVIN

At the suggestion of Dr Arthur Curtis, treatment with sodium paraaminobenzoic acid was begun March 29, tablets, 2 Gm, were taken every three hours during the waking hours The clinical improvement has been spectacular

DISCUSSION OF TWO PRECEDING CASES

Dr Hamilton Montgomery, Rochester, Minn With respect to Dr Mitchell's case, the photograph of the patient shows a definite reaction apparently to chaulmestrol which I have been using for some time in cases of mycosis fungoides but with, on the whole, indifferent results There have been 1 or 2 cases in which striking improvement occurred Dermatitis from the use of chaulmestrol is an unusual occurrence

Dr A C Curtis, Ann Arbor, Mich Two months ago, at the meeting here, Dr Mitchell asked whether I could suggest anything that might be of value in his 2 cases of mycosis fungoides In both cases the roentgen response had been exhausted I suggested that he might try para-aminobenzoic acid Dr Zarafonetis, a member of our medical department, and I have been using sodium para-aminobenzoate in the treatment of some of the lymphoblastomas Because of its relation to the local anesthetics we thought that it might have some value in certain of the lymphoblastomas Our patients received 2 Gm of the sodium salt every two hours around the clock Dr Mitchell gave 2 Gm of the acid every three hours around the clock Some of our patients had a Herxheimer reaction characterized by redness and burning of the lesions The reaction would subside, and often the lesions would disappear The first patient we treated was something like the one Dr Mitchell showed today, a woman with a psoriasiform type of mycosis fungoides The effect of roentgen rays had long been exhausted She also improved rapidly on treatment The drug is by no means innocuous It has many disadvantages when given in large doses One is that it produces glycosuria, which seems to be related to a lowering of the renal threshold because the patient often has blood sugar values that are relatively low, 40 or 50 mg per hundred cubic centimeters In 1 patient with psoriasis hypoglycemia of such severity occurred that treatment with the drug had to be stopped Some patients have nausea and some fatigue In 1 case we had to stop use of the drug because of the Herxheimer-like effect How it acts and whether its reaction will be sustained have not been determined

Dr H E Michelson, Minneapolis My co-workers and I have tried urethane in Kaposi's sarcoma with no effect We did have some effect with nitrogen mustard We also had temporary results with nitrogen mustard in mycosis fungoides

Dr Stephen Rothman It was interesting to note in this case that, while the premycotic lesions were highly pruritic, the tumors themselves do not itch In my experience this is the rule Pruritus is present as long as there is a defense reaction of the skin against the deposition of foreign cells After the infiltrating tumor has established itself and started unlimited growth, itching subsides

The experience with nitrogen mustards in Billings Hospital has been that about in 50 per cent of the cases of Hodgkin's disease the cutaneous manifestations react favorably The practical significance of this therapy is that it is effective in cases in which the beneficial effect of roentgen rays has been exhausted However, the final outcome has not been changed so far

Dr Edward A Oliver With reference to Dr Cornbleet's patient, I have watched the man for the last seven years He has been a constant attendant in our clinic at Northwestern University, and we have always presented the case as

one of psoriasis of the plaque type Itching is present, but I have seen Negroes with psoriasis who do have considerable pruritus He gets worse and gets better I examined the slides, and I do not believe that one could make a diagnosis of mycosis fungoides from them

DR ADOLPH ROSTENBERG (by invitation) What percentage of cases of parapsoriasis en plaque become cases of mycosis fungoides?

DR HAMILTON MONTGOMERY, Rochester, Minn In a fairly large series of cases that I studied with Burkhart (ARCH DERMAT & SYPH **46**.673-690, [Nov] 1942), we came to the conclusion that parapsoriasis remains as such and does not eventuate in mycosis fungoides Mycosis fungoides may start out looking like parapsoriasis and remain as such for many years, but when the cases are studied in the early parapsoriatic-like stage histologic changes of mycosis fungoides are already demonstrable, including clumping of cells, pyknosis, karyorrhexis and multiplicity of cell types in the infiltrate Dr Sweitzer and his associates have presented a case of supposed parapsoriasis many times in the course of the last fifteen years Dr Madden obtained numerous specimens of biopsy from the beginning, about fifteen in number Two thirds of these biopsy specimens revealed definite features of mycosis fungoides, and I anticipate that this patient eventually will have all the clinical features of that disorder

DR S W BECKER I distinctly remember the late Professor Bloch saying that Brocq had abandoned the term erythrodermie pityriasique en plaque disseminée He said that he no longer held to the belief that there was a type of parapsoriasis to which he gave this name

DR OTTO H FOERSTER, Milwaukee There now are perhaps about a dozen undisputed cases of parakeratosis variegata on record The disease in several of the original cases, when seen again at a later time by Unna, was found to have undergone a clinical change and was recognized by him as mycosis fungoides

DR THEODORE CORNBLEET The initial lesion that my patient showed was a well developed tumor, which classified his disease as the d'emblee variety Subsequently there was regression to the second, or infiltrative, stage with extensive lesions Thus various stages may be present simultaneously, and their mode of evolvement and progression may follow different patterns A patient at the Cook County Hospital was treated recently with the relatively new nitrogen mustard method In a disease with a course as capricious as mycosis fungoides it is difficult to be sure, but this form of therapy seemed to have hastened this particular patient's death An autopsy was made, and the heart, liver and other viscera were found to have heavy infiltrates with characteristics of granuloma fungoides Some of the newer fission products may improve the prognosis in the lymphoblastomas, though thus far they have not done what could not be achieved with the older radiation modalities

Sarcoidosis. Presented by DR S ROTHMAN and (by invitation) DR E L LADEN

M H, a Negro woman aged 31, is a seamstress whose illness began in 1942 with a nodular lesion on her left upper arm This increased in size, and new lesions appeared on her face, right arm and left leg in the intervening years

In 1943 she suffered from short-lasting attacks of pain in the left ankle and knee This disappeared spontaneously after ten months In November 1946, she noted swelling of the proximal phalanx of the third finger, right hand This has become progressively worse

The patient was seen by the Chest Department of the University of Chicago Clinics in February 1945 Results of tuberculin skin tests with dilutions of

A Case for Diagnosis (Psoriasis? Lichen Planus?) Presented by DR REES B REES

Xanthoma Diabeticorum Presented by DR PAUL FASAL

A Case for Diagnosis (Endothelial Tumor? Angioblastoma?) Presented by DR HARRY E ALDERSON and DR CHARLES ALBERT SHUMATE

C W, a white man aged 66, presents a well outlined, dark blue patch, 4 cm in diameter, superior and posterior to his left eye Surrounding this area and extending over most of the left cheek is a hard, somewhat puffy, violet discoloration (ecchymosis) The areas are painless On the anterior frontal region are two crusted keratotic lesions There is ptosis of his left lid His serologic test for syphilis gave negative reactions

A report from Dr Ream Leachman, of Vallejo, stated that Dr Medley, an oculist, examined the patient's eyes and reported that the lesions of the left lid were noninflammatory and that the ptosis was from their weight The eyeball was normal The vision, orbital contents and fundi were normal

As we believed that the disease might be the result of neurotrophic changes in the trigeminal area, for example, due to thrombosis of the posterior inferior cerebellar artery, the patient was referred to Dr Edmund Morrisey (neurosurgeon) for consultation He reported that there were no neurologic changes of significance

The histologic sections were examined by Dr Wilbert Sachs, of New York He reported that throughout the middle and upper parts of the cutis in one portion of the slide were numerous blood vessels and spaces and an intense cellular infiltration of angioblasts The surrounding tissue and overlying epidermis showed no important change The cells had large round, fairly well stained nuclei and either no cytoplasm or only a slight amount The diagnosis from microscopic study was some type of endothelial tumor, belonging to the angioblastoma group

Favorable Response of Tuberculosis Cutis (Lupus Vulgaris) to Therapy with Vitamin D Presented by DR REES B REES

A Case for Diagnosis (Multiple Areas of Superficial Atrophy of the Trunk Macular Atrophy?) Presented by DR H V ALLINGTON

Coccidioidal Granuloma on the Cheek Presented by DR OTTO E L SCHMIDT

A Case for Diagnosis (Generalized Papular and Nodular Eruption Present at Birth) Presented by DR H V ALLINGTON

C M C, a 4 month old Negro baby girl, except for her skin, was a normal full term infant weighing 5 pounds 8 ounces (2,495 Gm) She has grown and developed in an average manner She has one normal 3 year old sister There is no history of similar cutaneous trouble in her family

At birth she presented a generalized papular and nodular eruption, with lesions varying in size up to 1 5 cm in the largest diameter These were firm

given Apparently the antireticular cytotoxic serum stimulates the reticuloendothelial tissue

DR W H GOECKERMAN, Hollywood, Calif Regarding the case presented by Dr Keddie, I cannot tell you what the name of the condition is, but certainly it is not papulonecrotic tuberculid This patient has none of the characteristics of Hodgkin's disease of the skin We must allow for other possibilities In this young man the process has been present for years and years, and yet it disappears when exposed to the sun rays systematically What it is, I do not know It seems to me an interesting picture, but I am sure it is not papulonecrotic tuberculid The papulonecrotic tuberculids have a characteristic picture I have seen a great many of them

DR GRANT MORROW, San Francisco I should like to comment on the case of Dr Ingels' (multiple benign pigmented fibroma) I think it is benign melanoma We had 2 patients recently in whom lesions developed on the dorsum of the feet Both showed melanoma of benign variety

DR FRANCES A TORREY, San Francisco Concerning the case of malignant thymoma that I presented, the diagnosis was made only after examination of several biopsies I understand that thymomas are rare, and Douglas Symners (Malignant Tumors and Tumor-Like Growths, Ann Surg **95** 544, 1932) reported 25 malignant tumors or tumor-like growth of the thymic area in 17,000 autopsies (0 14 per cent) from the Pathology Laboratory of the Bellevue Hospital Hamberger (*Arch Path* **36** 37, 1943) reported that in 6,000 autopsies there were found 41 instances of tumors or enlargement of the thymus Of these only 3 were found to be malignant Under the classification of thymoma five types of malignant growths may occur (1) perithelioma from connective tissue of the walls of the blood vessels, (2) lymphosarcoma from the lymphocytic elements, (3) epithelioma from the epithelial reticulum cells, (4) spindle cell sarcoma from the connective tissue framework and (5) Hodgkin's disease from lymphocytes in the thymus Of these five, lymphosarcoma and Hodgkin's disease are the most radiosensitive This tumor was considered to be of the Hodgkin type after the first biopsy was made, and it was treated accordingly The tumor did not show any regression until after the diagnosis of epithelioma was made and the large dosage of roentgen rays was given Although the regression of the tumor has been remarkable, the prognosis, of course, is extremely poor There was a large, widely infiltrating lesion of the mediastinum that spread by direct extension to the axillas It is amazing that there has been no sign of metastasis, only the spread by direct extension

DR ARNE E INGELS, San Francisco My case was presented with the idea of clarifying the diagnosis For the pathologic diagnosis increased vascularity only does not satisfy, obviously I even thought the condition resembled pseudoxanthoma elasticum histopathologically The predominant feature was a great increase in elastic tissue, even clumping and homogenization However, clinically it did not correspond to this Otherwise, it might be a more benign xanthoma The tumor was treated with roentgen rays years ago and lost the picture of unusual singular blackish melanotic pigmentation The remaining tumor on the dorsum of the foot still retains the pigment Microscopically, it shows basal cell melanin changes within the normal So, what can it be but a benign tumor of elastic origin?

DR FRANCES M KEDDIE, San Francisco The condition of the student may not be Hodgkin's disease Clinically it does not fit with the histologic examination I had a note from Dr Hamilton Montgomery, who said it looked like malignant lymphoma The description was made by Dr Bostick, who has been interested in Hodgkin's disease for a long time I met Dr Bostick in the hall just now, and he told me he feels fairly certain it is Hodgkin's disease

The larger ones appeared to be made up of conglomerate masses of smaller ones They were, for the most part, a normal cutaneous color Some were slightly paler They seemed nontender and showed none of the signs of an inflammatory process

Since birth the lesions appear to be slowly disappearing Many of the smaller ones seem to have disappeared The largest ones are on the scalp, and several of these are a faint xanthomatous yellow, which was not so notable earlier When I last saw the baby I thought I could feel an enlarged firm nontender spleen This was not confirmed by a pediatrician who subsequently examined her

A biopsy, Aug 7, 1946, was reported by the pathologist to show stratified squamous epithelium with normal subcuticular structures In one margin of the section the subepithelial tissue was infiltrated by monocytic series cells consisting of lymphocytes and plasma cells This process extended into the deepest layers of the skin and was a diffuse rather than a dense pattern

The Kahn and Wassermann reactions were negative at birth The Kahn and Kline reactions were again negative on November 9 The cholesterol content of the blood was 150 mg per hundred cubic centimeters on November 9 The hemogram and the differential count were essentially normal

DISCUSSION

DR MERLIN T-R MAYNARD (San Jose) Is there any history of bromide ingestion in the mother?

DR H V ALLINGTON I did not question her about that

DR REES B REES I think that the occasional tremendous activity of the sebaceous glands in young children is of interest It is observed in clinics in normal babies, and babies go through that period without much difficulty

DR H V ALLINGTON I did not get the impression that the sebaceous glandular apparatus was involved I considered the possibility of its being a lymphoblastoma Also, because of the yellowish color in several of the scalp lesions at the present time, I wonder about this being another case of nevoxanthoendothelioma It is possible that if a biopsy specimen were to be taken from one of the scalp lesions at the present time, it would show a more characteristic picture

JOINT MEETING OF THE SAN FRANCISCO, LOS ANGELES AND PACIFIC NORTHWEST DERMATOLOGICAL SOCIETIES

Ervin Epstein, M D, *Presiding*

Jan 18, 1947

A Case for Diagnosis Pemphigus Vegetans? Presented by LIEUT COL ROBERT S HIGDON, Letterman General Hospital, San Francisco (by invitation)

Lupus Erythematosus or Dermatomyositis? Presented by DR EDWARD LEVIN

A Case for Diagnosis Unusual Fragility of the Skin (Related to Epidermolysis Bullosa or Ehlers-Danlos Syndrome) Presented by DR HARRY J TEMPLETON, Oakland, Calif

Epidermolysis Bullosa Presented by DR NORMAN N EPSTEIN

Sjogren's Syndrome Presented by DR H V ALLINGTON, Oakland, Calif

A G, a white woman aged 63 years, has had dryness of the mucous membranes of her mouth and eyes since 1934 This has become so severe that she has to wet her mouth with water to enable her to talk Her eyes are so dry and sticky in the morning that she has to wash them with water to get them open There are also periods when she appears to have an excess of a sticky and tenacious mucus in her mouth Her symptoms started at about the time of her menopause She has had the usual diseases and also had erysipelas and pneumonia when she was a child In 1927 she had a "nervous breakdown," which was thought to be from overwork Severe attacks of arthritis began about 1937, and she has had recurrences since then lasting from three to four days but apparently decreasing in severity as time goes on A systolic blood pressure of from 170 to 200 mm of mercury has been present for years

There are no objective changes in the mucous membranes The lacrimal glands are not palpable The salivary glands are small but palpable and are not tender

There is clubbing of the finger nails and mild hypertrophic changes in the small joints of her fingers The blood pressure was 200 systolic and 100 diastolic The reaction to the Schirmer test was 7 mm in 5 minutes (normal 21 to 25 mm) Her eyes otherwise were reported normal by Dr J R Sharpsteen, Oakland, Calif, except for a mild defect of conversion The blood count and urinalysis were essentially normal

A vitamin A concentrate of 25,000 units, given three times daily, has been of no benefit Hormones have not yet been tried

DISCUSSION

DR W H GOECKERMAN, Hollywood, Calif The last case interests me more than anything I have observed in years but not because it was called "Sjogren's syndrome," since I do not know whether that means anything If the patient came into my office and told me of the dryness of her mucous membrane, I would not know how to approach the case I went further into the history and talked at some length to the patient She told me that she does not know if she has any coldness in her fingers Her friends have told her that her hands are cold I saw that she had a peculiar sort of erythematous livid condition of her fingers There is a definite vasomotor disturbance, secondary disturbance of nutrition to the finger nails My first thought would be to give her estrogen I think it is not uncommon to see vasomotor disturbance in those along in years, even up into the seventies, as the result of endocrine imbalance I should like to suggest that a systematic effort be made to give estrogen therapy in this case under whatever name you may call it This is to me a mild disturbance which we frequently see for years following the menopause

DR SAMUEL AYRES JR, Los Angeles Perhaps there is some disturbance in the involuntary nervous system Pilocarpine, 1/20 to 1/10 grain (3 to 6 mg) three times daily, might affect the stimulation of the salivary glands and perhaps will stimulate the production of tears

A Case for Diagnosis (Behcet's Syndrome? Pemphigus?). Presented by DR JOHN M GRAVES

V H, an American woman aged 52, was presented at the meeting of the San Francisco Dermatological Society on Nov 15, 1946

Verrucous Lupus Erythematosus? Nevus Verrucosus? Presented by DR STUART C WAY and DR JAMES R DRAKE

Lupus Erythematosus, Accentuated by Solar Sensitivity. Presented by DR ARNE E INGELS

Tuberculosis Verrucosa Cutis Presented by DR STUART C WAY and DR JAMES R DRAKE

Keratoderma of Buttocks (Syphilitic or Pyogenic? Psoriatic?) Presented by DR WILLARD M MEININGER

Maduromycosis Presented by DR HIRAM E MILLER

Subcutaneous Granuloma Annulare? Presented by DR HIRAM E MILLER

S S is a 4 year old girl Her mother stated that seven months previously she noticed a small lump under the skin on the lower part of the patient's right leg and on the extensor surface of the right elbow These areas have become progressively larger in size

The physical examination reveals two rather diffuse, cherry-sized, firm, subcutaneous nodules, not freely movable and nontender, with no overlying cutaneous changes, located on the extensor area of the right elbow and on the anterior surface of the lower part of the leg

In July 1946 roentgen ray examinations showed no pathologic bony changes in the right tibia and fibula, the right elbow and forearm or the skull In September 1946 there was noted increased density in the soft tissues of the right elbow The density was sharply outlined and homogeneous and appeared to conform to the position of the supinator muscle No evidence of abnormality was seen in the bones of the forearm In the roentgenograms of the right tibia and fibula there was a localized swelling of the soft tissue situated anteriorly over the tibia, in the region of the junction of the upper and middle thirds, but the bone structures of the tibia and fibula were normal In November 1946 there was increase in the size of the mass on the anterior superior surface of the right tibia The density in the left elbow was less definite

Agglutination reactions for brucellosis were negative The tuberculin cutaneous test gave a negative reaction The sedimentation rate was 8 mm per hour The hemogram showed 4,450,000 erythrocytes and 5,100 leukocytes, with neutrophils 10 per cent, lymphocytes 86 per cent and monocytes 4 per cent

On Dec 4, 1946, a biopsy was performed on the nodule of the right leg The specimen consisted of an incised piece of yellowish gray tissue of elastic consistency with some surrounding connective tissue It measured 1 4 by 1 2 by 0 9

DR H V ALLINGTON, Oakland, Calif This is the third patient whom I have recently seen with the complaint of dryness of the mucous membranes of the eyes, nose and mouth This problem has been discussed in the American literature by ophthalmologists more than by dermatologists (MacLean, A L Sjogren Syndrome, *Bull Johns Hopkins Hosp* **76** 179-191 [May] 1945, Freedman, B, and Gerrard, H Sjogren's Syndrome Treated with Stilbestrol, *California and West Med* **64** 31 [Jan] 1946), deRoetth, A Hypofunction of the Lacrimal Gland and the Sjogren's Syndrome, *Lancet* **65** 423-425 [Dec] 1945) It has been reported as occurring in women after the menopause It has usually been associated with other diseases, especially arthritis or focal infection In some patients there has been a swelling of the salivary and lacrimal glands early in the course of the disease, with atrophy later The changes in the eyes may be marked, sometimes progressing to a severe keratitis and corneal erosions

Vitamin A deficiency has been suspected, and administration of vitamin A has been reported as helping in some cases It made no difference in this patient and in 1 other whom I have seen

Because of its association with the menopause, an endocrine background has been suspected, and the administration of stilbestrol has been reported as helping temporarily

Scleroderma Circumscriptum and Morphea Guttata Presented by DR CHARLES W MCNITT, Reno, Nev

Localized Scleroderma Presented by DR FRANCES A TORREY

Scleroderma? Diabetes Mellitus Syphilis of the Central Nervous System? Presented by DR JULIAN C LUNSFORD, Oakland, Calif

Scleroderma Presented by DR DAVID BOHR (by invitation)

Scleroderma Presented by DR DAVID BOHR (by invitation)

Poikiloscleroderma with Calcinosis Presented by DR FRANCES A TORREY

Calcinosis Cutis Presented by DR HIRAM E MILLER

DISCUSSION

DR WALTER R NICKEL, San Diego, Calif The case of a single lesion on the back (localized scleroderma, presented by Dr Torrey) I think is a case of lichen sclerosis et atrophicus There is definite plugging in the central portion of the lesion The condition of the man with stiffness of his hands and forearms I would say resembles more closely acrosclerosis There is typical sclerosis of the "V" of the neck area, along with inability to open his mouth fully or produce wrinkling of the forehead

DR D E H CLEVELAND, Vancouver, B C Are there any further suggestions as to treatment? In 1 case of acrosclerosis and scleroderma I have used 150,000 units of calciferol (vitamin D_2) daily The patient thinks he is better, but I do not think he is

DR NELSON PAUL ANDERSON, Los Angeles Etamon chloride® (tetraethyl ammonium chloride), a new drug produced by Parke, Davis and Company, is being used at the University of Michigan for peripheral vascular disorders It is

cm The sections revealed a young-appearing mesenchymal connective tissue and surrounding fat, both containing numerous endothelium-lined vessels and a mild inflammatory reaction There were several focal areas of necrotic degeneration with surrounding pseudopalisading of cells There were also bits of eosinophilic intercellular material suggesting the presence of fibrosis The diagnosis was "subcutaneous nodule consistent with rheumatic nodule or with granuloma annulare"

No treatment was given

Erythema Annulare Centrifugum Presented by DR ERVIN EPSTEIN

Sickle Cell Anemia with Ulcers on the Legs Presented by DR NORMAN N EPSTEIN

DISCUSSION

DR HIRAM E MILLER, San Francisco My case is presented as an example of subcutaneous granuloma annulare This is the second patient that we have seen with this condition in the past year The lesions in both cases were firm, subcutaneous, nontender and cherry sized and were tightly bound down to the deeper structures The focal areas of coagulation necrosis with a palisade-like arrangement of the infiltrate seem to be compatible with the diagnosis Grauer and Wile described this variant of granuloma annulare in the ARCHIVES (**30** 785, 1934)

DR ERVIN EPSTEIN, San Francisco In the patient with erythema annulare centrifugum the lesions change a great deal from week to week I have been seeing her for more than a year, so I can make this statement with certainty The condition appeared entirely different one week ago At one time it was thought that the condition might be granuloma annulare, but further observation has established the present diagnosis This histologic picture is consistent with erythema annulare centrifugum At first the possibility of a phenolphthalein eruption was also considered, but the discontinuance of the use of this drug for the past year has not resulted in a lessening of the activity of the condition The patient has had a great deal of treatment, with little benefit However, sulfadiazine by mouth has repeatedly resulted in prompt clearing of the eruption Discontinuance of administration results in just as prompt recurrences

DR NORMAN N EPSTEIN, San Francisco In our experience sickle cell anemia is rare The subject was well covered by Cummer and La Rocco in 1940 Certain interesting points relating to this condition might be mentioned The name "sicklemia" probably fits the condition much better because people with sickling of their red blood cells are not always anemic Many of them go into periods of profound anemia, and later their blood may regenerate to a normal condition The anemia may be transient in this group of patients It is a condition primarily found in Negroes but is not absolutely restricted to that race Some cases have been reported in the white race, among Sicilians and Mexicans About 8 per cent of Negroes have sickling of their blood I do not know in what percentage anemia develops The anemia found is of the hemolytic type Ulcers are one of the symptoms Other symptoms may be referable to the liver, heart, spleen and other viscera The origin of the ulcers is well understood They are peculiarly shaped It is not a specific ulceration as far as one can determine Whether it is due to the anemia is a question Certainly, in other severe anemias ulcers of the legs are not reported frequently But in 75 per cent of the patients with sickle cell anemia these ulcers do occur They are probably due to trauma plus

supplied for experimental use only At the University of Michigan they have used it in this group of peripheral vascular diseases, including Berger's disease In 1 personal case of Raynaud's syndrome with scleroderma-like changes in the skin, together with definite ulceration and impending gangrene, I felt that amputation would be required shortly The patient improved after therapy with this new drug, and the affected digits apparently have been saved Persons so treated should not drive a car for several hours as there is prompt interference with visual accommodation While I do not feel that this drug by any means solves the problem of peripheral vascular disease, yet it is to be considered for use in persons who have ulceration, impending ulceration or early gangrene of digits

DR NORMAN N EPSTEIN, San Francisco In the case of generalized scleroderma (presented by Dr Bohr) the condition was severe when the patient first came into the clinic It was so severe that he could hardly open his mouth He was given artificial fever therapy With this, he improved A second patient came in at the same time with a condition which was almost identical and was also given fever therapy This woman did not improve We have not tried fever therapy in many cases, but I think it has benefited that man Certainly, it increased the basal metabolism and increased the blood flow to the skin I think it is worth while to try the artificial fever therapy, once a week for ten weeks, in cases of this type

DR FRANKLIN I BALL, Hollywood, Calif With regard to the diagnosis of scleroderma in a patient who is diabetic (case presented by Dr Lunsford), if this is an instance of scleroderma, it is certainly not the usual picture which one expects to see I was much more impressed with the possibility that this was an instance of degeneration of the connective tissue elements of the skin, possibly amyloidosis cutis

DR W H GOECKERMAN, Hollywood, Calif I am interested in that woman whose lesions were essentially unilateral (case presented by Dr McNitt) I would suggest the diagnosis of lichen albus For years there has been discussion as to whether lichen albus belongs to the lichen planus group We got away from that conception, but where it does belong I do not know I still hold that lichen albus is a disease entity, not of the same nature as any form of scleroderma or of lichen sclerosis et atrophicus The cause is entirely obscure

DR WALTER R NICKEL, San Diego, Calif There is no evidence of lichen sclerosis et atrophicus in the girl The upper layer of the corium showed typical sclerosis, with atrophy of the appendages, without the homogenized edematous character of lichen sclerosis I think it is a pure case of unilateral scleroderma

DR REES B REES, San Francisco I agree with the last speaker

DR CHARLES W MCNITT, Reno, Nev I believe this interesting group might well form a small symposium on so-called scleroderma I should like to invite you away from the use of that term entirely There will come a time when we will all agree with the conclusions made by Goetz in the "1945 Year Book of Dermatology and Syphilology" that this type should be called multiple progressive systemic sclerosis He does not think that we should call it scleroderma Other interested workers bore out the vascular factor and called it angiitis Some day we may say that Raynaud's disease and dermatomyositis belong in the same group I am willing to admit my ignorance, but I think we should take that broad view In 1928 Allen, in the ARCHIVES, described the same morbidity, edema, cellular infiltration, fibrosis and subcutaneous atrophy in the skin in scleroderma, in dermatomyositis scleroderma and in dermatomyositis, and stated that in all there are the same prodromal symptoms, frequent history of rheumatism, rheumatic fever and other evidences of focal infection, which relates them closely

secondary infection in a patient who has a lowered resistance due to the anemia The 6 month pregnancy in this woman is an unusual finding Only 3 cases of pregnancies carried to term in this group of patients have been reported The patients in these cases had had miscarriages some years before The pregnancy in this patient has gone on in a fairly normal manner Pregnancy may be dangerous for her since severe toxemias have occurred in pregnant women with sickle cell anemia, at times leading to a fatal termination

Multiple Benign Cystic Epithelioma Presented by Dr Edward Levin

Syringocystadenoma Presented by Dr Frederick G Novy Jr

DISCUSSION

Dr Nelson Paul Anderson, Los Angeles I appreciate having observed this group of cases I should like to comment on the case presented by Dr Novy as one of syringocystadenoma I think that is undoubtedly the correct diagnosis Many different terms have been applied to this condition Syringocystadenoma, I think, is primarily a benign adenomatous condition, involving the sweat ducts and glands It is fairly common about the lower eyelids and the axillas I do not know why the term "syringoma" is sometimes used Pollitzer's translation of Darier's book has a photograph labeled syringoma, showing involvement of the lower eyelids I do not think that biopsy is ordinarily done when the condition occurs on the lower eyelids

The case presented by Dr Ervin Epstein as one of multiple cutaneous neuromas is the first case of this condition I have ever observed, and I was not able to make a clinical diagnosis I have seen 2 cases, 1 with a solitary nodule and the other with three or four discrete nodules which clinically appeared to be fibromas However, this diagnosis could not be confirmed histologically

There was a report by Wile and Montgomery several years ago of extensive involvement of one of the breasts in a woman As I recall it, pain was a marked clinical feature

Dr Werner W Duemling, San Diego The case that interested me most in this group was the rare case of cutaneous neuroma, and I should like to emphasize the word "rare" The case which Dr Anderson credited to Dr Montgomery was the case which I reported in the Archives in February 1929 The condition, as I remember, was first described by Duhring My case was the fifth reported in the literature Birchoff straightened us out on the histology of this lesion and pointed out that there are two types of cutaneous neuromas, the true and the false The true type, of course, is made up of medullated and nonmedullated bundles of nerve fibers intertwined or interlaced, much as we saw in this section In the false type the fibers arise from neurilemma In the case which I presented the lesion involved one half of the breast area and was dull brownish red in color and extremely sensitive Special stains revealed it to be a true neuroma The patients always complain of pain and hyperesthesia

Dr Hiram E Miller, San Francisco The patient with cutaneous neuroma without pain is of particular interest to me As far as I can recall, the few patients whom I have seen or have read about have had pain There is a report by Kyrle in Ormsby's textbook (1943) on a similar lesion without pain, described as "unripe" neuroma to account for the absence of pain

The types presented today run the gamut of scleroderma types, except for the "cardboard" form Scleroderma circumscriptum may be found with a widespread or general distribution and should not be classed as "localized" Also, diffuse scleroderma requires a better term than generalized scleroderma, as it is often confined to places such as the hands, forearms, feet and legs or face and neck The use of "white spot disease" has largely been given up, because it led to confusion between lichen sclerosis et atrophicus and morphea

The woman of 27 years of age (presented by Dr McNitt) in whom there was a relatively gradual onset of scleroderma is interesting because of the possibility of an etiologic endocrine factor associated with her pregnancy The condition is largely limited to one side She was found to have apical abscess of the second molar and an impacted wisdom tooth They should be cared for These patients often improve greatly after focal infection has been removed She has had no history of exposure to arsenic While the condition originally progressed steadily, with greater and greater spread of the lesions, she has improved on the following medication thyroid extract, 3 grains (0 2 Gm) daily, 150,000 units of vitamin A and a pancreatic extract in the form of padutin ®

To my mind this case is definitely one of scleroderma and morphea guttata Histologically, the atrophic epithelium and the hypertrophic collagen bundles characteristic of scleroderma are present The picture of lichen sclerosis et atrophicus is not present

DR HIRAM E MILLER, San Francisco I think it should be pointed out that in the case presented by Dr Bohr (S W) sympathectomy was done without any benefit I should like to state also that the large biopsy scar was the result of the surgical removal of a large piece of tissue for chemical studies

In the case presented by Dr Torrey as one of poikilosclerodermа with calcinosis there is no doubt about the diagnosis It was presented here at the last meeting in 1939

In my patient, unfortunately, all the lesions were excised except one on the left knee In both instances calcinosis cutis was of circumscribed variety

Ervin Epstein, M D , *President*
Frances M Keddie, M D , *Secretary-Treasurer*
March 21, 1947

Recalcitrant Pustular Acrodermatitis of the Hands Presented by DR J M READ (by invitation, for DR OTTO E L SCHMIDT)

Erythema Perstans Presented by DR HARRY J TEMPLETON

Hansen's Disease Presented by DR J M READ (by invitation, for DR OTTO E L SCHMIDT)

Basal Cell Epithelioma, Morphea-Like Sclerosing Type in the Nasolabial Fold Presented by DR FRANCES A TORREY

Lichen Sclerosus et Atrophicus of the Female Breast Presented by DR ARNE E INGELS

DR ERVIN EPSTEIN, Oakland, Calif The interesting feature in the case of multiple neuroma, of course, is the rarity of this condition In reviewing the literature, one is impressed by the repeated history of trauma preceding the lesions The patient refused to allow surgical intervention, so roentgen therapy is being attempted Despite the fact that nerve tissue is considered to be relatively insensitive to radiation, even one treatment of 200 r produced some improvement

Circumscribed Myxedema of the Legs Presented by DR STUART C WAY and DR JAMES R DRAKE

A Case for Diagnosis Nevoxanthoendothelioma? Presented by DR H V ALLINGTON (From the Berkeley Hospital Clinic, Berkeley, Calif)

The case of G M C, a 6 month old Negro baby girl, was presented on Nov 15, 1946, at the meeting of the San Francisco Dermatological Society

Nevoxanthoendothelioma Presented by DR MAX E KRAUSE

The case of G T, a white boy aged 9 months, was presented at the meeting of the San Francisco Dermatological Society on Nov 15, 1946 Thus far there have been no signs of regression of the lesions

Necrobiosis Lipoidica Diabeticorum Presented by DR FRANCES M KEDDIE

DISCUSSION

DR NELSON PAUL ANDERSON, Los Angeles Localized myxedema may come on acutely and be so inflammatory as to mislead the thyroid surgeon and the cardiologist I have seen one instance of localized myxedema in a Chinese leper who had undergone thyroidectomy In a recent article, someone writing on the subject of leprosy described lesions of this type occurring in connection with it

Necrobiosis lipoidica diabeticorum was first described as a clinical entity in the latter part of the third decade of this century I should like to call your attention to an article in the *American Journal of Medical Sciences* (Goldstein, E, and Harri, J Xanthoma Diabeticorum An Unusual Process of Evolution, *Am J M Sc* 173-195 [Feb] 1927)

DR MERLIN TREVOR-ROPER MAYNARD, San Jose, Calif For the Negro child with the diagnosis of nevoxanthoendothelioma I should like to offer the diagnosis of urticaria pigmentosum In this child wheals would definitely be produced after stroking I think that a biopsy and stains for mast cells should be made, which are characteristic of this condition

DR J WALTER WILSON, Los Angeles I too should like to follow Dr Maynard's suggestion as to the diagnosis in the case which Dr Allington presented under the title of "nevoxanthoendothelioma" I think that the correct diagnosis is urticaria pigmentosa I was interested in the conversation with the mother, who states that whenever the child is rubbed, wheals appear in "little spots" I tried to elicit the sign known as "Darier's sign," in which friction produces whealing limited to the pigmented areas I do not believe that this can be demonstrated

Pityriasis Rubra Pilaris of Nine Months' Duration in a Woman 62 Years of Age Presented by DR FRANCES M KEDDIE

Dermatomyositis Presented by DR J M READ (by invitation, for DR WILLARD M MEININGER)

O McC, a 26 year old white American housewife, has had frequent sore throats and earaches since the age of 15 years She had taken sulfonamide drugs and penicillin frequently in the past three years One and a half years ago she first noted muscle stiffness in her arms, legs and neck, which was not associated with any infection of the upper part of the respiratory tract About four months ago the stiffness became worse and gradually increased to cause almost complete invalidism Cutaneous swellings appeared, and the skin became tight and hard and sensitive to heat and to touch The facial edema and difficulty in swallowing began three weeks ago

Numerous erythematous plaques and patches are seen on her trunk and the proximal portions of her extremities A brawny induration of the muscles seems to attach them to the overlying skin

The results of a urinalysis and a hemogram were normal The result of the heterophil agglutination test was normal The serologic reaction for syphilis was negative The roentgenograms of the chest, elbows and hands revealed no abnormalities The chemical content of the blood per hundred cubic centimeters was cholesterol 250 mg, calcium 10 mg, inorganic phosphorus 4 2 mg, total proteins 6 0 mg, albumin 4 4 mg and globulin 1 6 mg The basal metabolic rate was +13 6 per cent

A section of the epidermis and a bit of adjacent muscle showed occasional small collections of lymphocytes about small arterioles, but no eosinophils and no evidence of tissue destruction or involvement of the arteriolar walls The diagnosis was focal, chronic myositis and chronic, mild dermatitis

DISCUSSION

DR FRANCES M KEDDIE I would like to suggest the diagnosis of periarteritis nodosa The patient has had episodes of diarrhea, but none of the stools was bloody These were often accompanied with fever for about four days She has been receiving sulfonamide drugs intermittently during that period There are nodules on the ulnar aspect of the right forearm which might be compatible with a diagnosis of periarteritis nodosa This seems to belong in that group of cases in which Rich and his associates were doing experimental work on rabbits Rich administered horse serum to the rabbits and also gave sulfonamide drugs and was able to produce the lesions of periarteritis nodosa A biopsy of one of these nodules on the patient's arm might confirm this diagnosis

DR HARRY E ALDERSON It would be unusual for a person with periarteritis nodosa to survive after three years

DR FRANCES M KEDDIE More cases of chronic disease are being recognized now

DR ERVIN EPSTEIN Dermatomyositis, periarteritis nodosum, scleroderma and disseminated lupus erythematosus may be classified in a single group There is considerable overlapping between these entities It is often difficult to separate these conditions clinically

DR WILLARD M MEININGER The onset and course of this condition were characteristic of dermatomyositis The patient first noticed stiffness in her legs,

Thymoma Presented by DR FRANCES A TORREY

The case of J N S, a 36 year old white woman, was previously presented before the San Francisco Dermatological Society on April 26 and Sept 13, 1946

Since the last presentation the following roentgen therapy was given From Sept 16 to Oct 3, 1946, a total dose of 3,000 r was delivered to each of two fields, the right and left axilla, with a filtration of 0 25 mm of copper and 1 mm of aluminum From Nov 19 to Nov 27, 1946, an area measuring 2 5 by 6 cm in the anterior cervical region was given 2,400 r with a filtration of 0 25 mm of copper and 1 mm of aluminum From Jan 20 to Feb 11, 1947, an area in the left cervical region measuring 7 by 7 cm received 3,000 r with a filtration of 0 25 mm of copper and 1 mm of aluminum



Thymoma in J N S

A Case for Diagnosis Multiple Benign Pigmented Fibroma Presented by DR ARNE E INGELS

D D, a white married woman aged 48, had had a lesion on her heel which started at the age of 15, a lump on the dorsum of the foot and one on the right forearm There was a gradual increase in the size of the tumor of the Achilles tendon, until it was 4 to 5 cm in diameter by June 29, 1945 The two other lesions increased slowly in size They have been brownish-blackish in appearance all the time The tumor on the dorsum of the foot was flat, blackish-brownish and approximately 1 5 cm in diameter

areas of erythema on the trunk and proximal portions of the extremities and puffiness of the face and ankles Muscle biopsy showed mild dermatitis and myositis

I want particularly to get suggestions as to treatment The patient has had reactions to drugs in the past I thought that the condition was fairly closely related to scleroderma and gave her an insulin-free pancreatic extract, but her condition is unchanged

DR ERVIN EPSTEIN In 1 case of dermatomyositis I have gone through the gamut of therapeutic possibilities I have given adrenal cortical extract, penicillin, an insulin-free pancreatic tissue extract, glycine and ephedrine Now the patient is getting fever therapy The disease does not seem to be improving

DR GEORGE V KULCHAR As I recall, particularly in 1 case, pyrotherapy was the most effective form of treatment

DR FREDERICK G NOVY JR My impression is that the cutaneous changes fit in better with the diagnosis of dermatomyositis than of periarteritis nodosa

Acne Rosacea with Ocular Involvement Presented by DR J M READ (by invitation, for DR OTTO E L SCHMIDT)

A B, a 46 year old married white American woman, was first seen on March 17, 1945, because of a rash on her face of six to eight weeks' duration which has appeared in the spring and fall for the past eight to nine years For two weeks she has noted photophobia and redness of her eyes The photophobia has appeared every year in spring and fall, at the same time as the rash on the face She gave no history of atopy

The erythematous patches and the acneform pustules are confined to the central oval of her face The keratoconjunctivitis is more pronounced in her left eye Treatment has consisted of sulfur-resorcin lotion and riboflavin, 10 mg three times daily

DISCUSSION

DR HARRY J TEMPLETON This process is rather typical of rosacea keratitis, which has been described by ophthalmologists as yielding specifically to riboflavin therapy

DR HARRY E ALDERSON Naturally one would think of the possibility of achlorhydria It is seen fairly often in rosacea with acne and in the keratitis rosacea which this patient presents

DR REES B REES The ophthalmologists think that superficial fractionated roentgen therapy is of real value in this condition Perhaps 50 r, unfiltered, once a week for several weeks, might be beneficial

DR MERLIN T-R MAYNARD (San Jose) Along the line of therapy, one seems always to have trouble in getting a response I have a patient, a boy of 14 years of age, whose mother has had severe rosacea for many years This boy had grown to be 6 feet 4 inches (193 cm) tall When I saw him he had severe rosacea with large acne pustules and keratitis such as this woman has I gave him vitamin A, 100,000 to 150,000 units, 15 mg of riboflavin by mouth daily and 5 mg of riboflavin by injection every third day Within ninety days he was free of all symptoms, including the keratitis I think that this woman should be given active therapy along these lines

On the lower portion of the Achilles tendon there is a discolored, firm, sessile lesion, 3 cm in diameter, which is grayish-brownish pink It is freely movable and has no infiltrating growth The dorsum of the right foot shows a brownish black, slightly raised lesion, 1 5 cm in diameter, which is well defined and freely movable with no inflammatory changes On the right forearm is a scar from the excision of one of the lesions There is no glandular enlargement

The physical examination shows a healthy woman with abdominal scar formations from previous operations for cystic ovaries, appendicitis and peritonitis The scalp shows four atheromas On the left side of her face is a darkly pigmented mole

The Wassermann reactions were negative on repeated examinations The blood count showed 4,100,000 red cells, 79 2 per cent hemoglobin, 6,400 leukocytes, 78 per cent polymorphonuclear neutrophils, 18 per cent lymphocytes, 1 per cent eosinophils

Hodgkin's Disease of the Skin (Generalized Erythroderma with Scattered Papules) Presented by DR FRANCES M KEDDIE

A Case for Diagnosis Hodgkin's Disease of the Skin Presented by DR FRANCES M KEDDIE

G E, a 17 year old student, has had a papular eruption since he was 7 years old This eruption has recurred each winter and has cleared up each summer after about two weeks of exposure to the sun With each recurrence there have been more lesions which have gradually become larger in size

The eruption is polymorphous There are papules and firm pustules 1 to 2 cm in diameter These are in the skin and can be freely moved over the underlying tissue They heal with slight scarring Some are excoriated, but few cause itching The lesions are distributed on the trunk and on the extremities

The physical examination showed a normal healthy boy except for the cutaneous disorder The blood count and urinalysis gave normal results

Biopsy has been twice performed, and on each examination the histopathologic process was essentially the same (One section was made at the Mayo Clinic in May 1944 and the second at the University of California in December 1946) The second section is reported on by Dr Bostick as follows "Immediately beneath the epithelium and in the subpapillary dermis there was a proliferative reaction composed of large pleomorphic cells, often in the giant form and some of them with prominent nucleoli There was a background of round cells, scattered fibroblasts, granular leukocytes and eosinophils The most proliferating and pleomorphic cells seemed to be of reticuloendothelial origin, and these extended in small groups down to the underlying dermis Careful examination with acid-fast stains, Giemsa stains and Gram stains showed no evidence of specific organisms"

A diagnosis of Habermann's disease was made in 1944, and the treatment that was given included administration of sulfonamide compounds, ultraviolet radiation and vitamins A and D in large doses None of these caused abatement of the eruption No roentgen therapy has been given

Mycosis Fungoides, Plaque Type Presented by DR FRANCES A TORREY

Mycosis Fungoides Pruritic Infiltrated Patches Presented by DR FRANCES A TORREY

I was disappointed in the results of treatment with riboflavin and vitamin A when I first used them In the absence of hydrochloric acid in the stomach, they have to be given in much heavier doses The response is always slow

DR OTTO E L SCHMIDT Riboflavin probably is specific for rosacea keratitis Patients respond to injections of riboflavin much better than to the oral administration of it

Frederick G Novy Jr, M D, *President*

Frances M Keddie, M D, *Secretary-Treasurer*

Sept 19, 1947

Recalcitrant Pustular Eruption of the Extremities Presented by DR REES B REES and DR EDWIN M HAMLIN (by invitation)

Cutaneous Hodgkin's Disease Presented by DR FRANCES M KEDDIE

O C, a white woman aged 48, was presented at the meeting of this society on Jan 18, 1947 From a biopsy of a lymph node from the left axilla the diagnosis was malignant lymphoma

A Case for Diagnosis (Psoriasis? Lymphoma?) Presented by DR FRANCES A TORREY

Lupus Erythematosus with Dissecting Pyoderma of the Scalp Presented by DR NORMAN EPSTEIN

Acrodermatitis Perstans Presented by DR ROBERT A STEWART

Vegetative Pyoderma Controlled with Streptomycin Presented by LIEUT COL ROBERT S HIGDON (by invitation)

Pemphigus Vulgaris Presented by DR REES B REES

Superficial Epitheliomatosis Presented by DR GRANT MORROW

DISCUSSION

DR H V ALLINGTON, Oakland In one case I prescribed podophyllin in isopropyl alcohol The patient was asked to use it daily if the reaction was not too severe It could not be applied every day because of irritation and soreness When the reaction became annoying, the patient would interrupt the treatment for a few days and then resume it When I last saw him the lesion had undergone involution to a great extent

Urticaria Pigmentosa in an Adult Presented by DR LEO COLUMBUS, Berkeley

Urticaria Pigmentosum Presented by DR ERVIN EPSTEIN, Oakland

Acrosclerosis Presented by DR GRANT MORROW

J M, a white man aged 42, was admitted to the Southern Pacific Hospital in August 1947 He complained of dull intermittent pain of two years' duration in

DISCUSSION

DR ERNEST K STRATTON, San Francisco, Calif Since reporting in 1942 the perimental transfer to mice from a patient with mycosis fungoides, I have made nilar transfers of tissues from 3 additional patients

The first was transferred on March 26, 1945 The case was far advanced at e time, and the patient died shortly thereafter All the animal inoculations have en negative to date The second, from 1 of the patients shown here this morning, is transferred on May 29, 1945 The specimen was placed in an icebox at 78 C for seven days It was then thawed and emulsified, and portions were jected into the brains of 6 mice and into the peritoneal cavity of another 6 One these mice (brain injected) died on June 10, 1946 (thirteen months after injec-in) Its liver was enlarged five times and its spleen enlarged twenty times icroscopic studies showed infiltrations similar to the picture of mycosis fungoides

The third transfer, from M J , was made on July 31, 1945 The tissue was st emulsified and then passed through a Seitz filter before being injected into mice intraperitoneally On May 6, 1946 (ten months after injection) 1 of the ice became ill and was killed Its spleen was ten times normal size Micro-opically it showed a mycosis fungoides type of cellular infiltration A portion this spleen was emulsified, and a second passage has been made

On July 31, 1945, when the first passage was made, whole blood from this tient was also injected intraperitoneally into 6 mice These mice were killed cently and their organs were normal The original emulsion from this patient as also inoculated onto the chorioallantoic membranes of eggs In 1 embryo mors developed on the eye and on the heart This type of reaction is being udied further

Another interesting observation in the last 2 cases was the fact that the mouse mors were produced by using a "cell-free" emulsion (in the case in which the ssue was Seitz filtered before injection) and a "dead cell" emulsion (in the case which the tissue was frozen for seven days before injection)

In view of these findings, it would seem that if there could be any correlation tween mycosis fungoides in the human being and that reaction which has been bserved in the mouse (in 3 cases out of 4), it would, I believe, favor the theory at the etiologic agent in mycosis fungoides is a toxin or a virus rather than a alignant tumor cell

DR D E H CLEVELAND, Vancouver, B C The most interesting point about ese cases of mycosis fungoides is the fact that the patients have had the disease r a length of time and yet are in excellent general health Also, only 1 of em, I believe, had had anything resembling the ulcerative lesions of mycosis ngoides, squashed-tomato-like tumors I also belong to that group who regard ycosis fungoides as a clinical and not a histopathologic diagnosis Udo Wile put in those words almost—mycosis fungoides is a clinical and not a pathologic entity eerman says that any case shown to be a manifestation of Hodgkin's or lympho-rcoma should be so named (*Am J M Sc* **211**:479, 1946) The histopathologic naracteristics are seen from time to time in other groups of lymphoblastomas ecently an autopsy on a patient whom I had had under observation with clinical ycosis fungoides for about two to three years showed the disease to be unques-onably giant follicular lymphoblastoma Antemortem biopsy of a lymph node owed the same Ulcerative lesions gradually developed

I have been studying our cases of malignant lymphoma in the Vancouver eneral Hospital for a ten year period Approximately 50 per cent of the patients ith Hodgkin's disease and 50 per cent of those with follicular lymphoma (giant llicular lymphoblastoma) had generalized erythroderma exfoliativa, in many lcerated In 1938 Dr Ormsby said, when observing 1 of these cases, "If I had

the back of his neck For two months he has had in the joints of his extremities a pain associated with coldness, weakness, swelling and hardening of the skin of his hands and feet In the past two months he has lost 20 pounds (9 Kg)

Examination shows the skin of the face, hands and feet to be hardened and edematous without pitting His hands and feet are cold, but the arterial pulses of both are good There is limitation of movement of about 20 per cent of the hands and feet

The Kahn reaction was negative The electrocardiogram showed a left axis deviation The blood cholesterol was 256 mg per hundred cubic centimeters, sugar 82 mg, urea nitrogen 8 mg, uric acid 4 mg and calcium 9 5 mg Repeated blood cell counts were within normal limits except on one occasion when the eosinophil count was 35 per cent. The roentgenograms of the chest, spine and pelvis showed no abnormalities Examination of the feces did not show blood and parasites

A stellate ganglion block was performed but effected no change Since Sept 3, 1947, seven injections of a pancreatic preparation (padutin®), each of 10 units, have made little difference

DISCUSSION

DR ARNE E INGELS The combination of padutin® with thyroid should be considered

DR EUGENE OSTWALD There is a difference between oral and muscular administration of padutin® I believe that the intramuscular administration is by far better and more effective Intramuscular injections can be given without any ill effect, and without reaction, once or twice daily for a long period of time

Papulonecrotic Tuberculid or Lupus Erythematosus? Presented by DR RICHARD O PFAFF, San Jose, Calif

Unexplained Edema of Nose Presented by DR FREDERICK G NOVY JR

Poikiloderma Vasculare Atrophicans (Jacobi) Presented by DR GRANT MORROW

R S, a white woman aged 54, born in Austria of Italian parentage, was first seen on June 9, 1947 She stated that itching of her arms and legs started six months ago and has gradually increased in severity On the skin of the arms and legs are symmetric, round, atrophic, 1 to 3 cm areas with telangiectasis The skin is dry and scaly The dermatitis simulates that of roentgen dermatitis

Physical examination showed the blood pressure to be 140 systolic and 80 diastolic There were no abnormal findings The blood cell count was within normal limits The Rumpel-Leede test showed increased capillary fragility The treatment has consisted of rutin (vitamin P), 60 mg three times a day The pruritus has greatly decreased The Rumpel-Leede reaction is now only slightly positive, and the patient feels much improved

DISCUSSION

DR EUGENE OSTWALD I would like to call this acrodermatitis chronica atrophicans, and I believe that the patient presents rather characteristic changes The skin at the elbows is bluish red, wrinkled and parchment like

not seen the slides, I would have called it mycosis fungoides" Jackson would have called it Hodgkin's granuloma Extensive cutaneous involvement does not present the picture as generally seen—great big lymph nodes in the neck The big nodes are chiefly in the axillas and groins

DR NELSON PAUL ANDERSON, Los Angeles I cannot agree with the diagnosis presented by Dr Ingels I believe that these lesions are really fibroxanthomas in which fat stains will undoubtedly show definite fat globules These give that peculiar yellowish color to the lesions, which was well shown in the one over the Achilles tendon You will not find xanthoma cells because the fibrotic tissue is predominant I do not think that they are ordinary pigmented fibromas

One patient with mycosis fungoides showed poikiloderma-like cutaneous changes on the anterior aspect of the trunk

Finally, I should like to call your attention to the more recent work dealing with mycosis fungoides and Hodgkin's disease More particularly, as dermatologists, we are interested in mycosis fungoides treated with nitrogen mustard Earl Osborne, of Buffalo, personally told of 3 cases of mycosis fungoides responding well to nitrogen mustard treatment Four cases at the Cedars of Lebanon Hospital in Los Angeles have responded with apparent involution of the tumors Two more patients are about to be treated, and 1 additional patient at the General Hospital is now being treated with nitrogen mustard Dr Ray Allington, who is acquainted with the cases at the County Hospital, might tell us of his experience with nitrogen mustard.

DR RAY ALLINGTON, Los Angeles I do not know the exact dosage recommended, but I believe it is given in small amounts in isotonic sodium chloride solution by means of intravenous drip and is given only three or four times on consecutive days to complete a single series One of the patients in our ward has had such a series of one of the nitrogen mustard preparations and has responded amazingly well Two of his lesions had been given roentgen therapy, but all were benefited by the drug We should like to see more patients so treated

DR FLETCHER HALL, Los Angeles Discussants so far have taken up all the cases in the group, except the case of Hodgkin's disease of the skin (?) presented by Dr Keddie, which I should like to introduce into the discussion I could not help but think of the diagnosis of papulonecrotic tuberculid when I first saw the patient Then, on reading in the history sheet what the Mayo Clinic said, I was thrown off the track I could not see any microscopic signs in the slide exhibited which would account for the clinical appearance of the lesions, and I wonder if it was a truly representative section of one of the lesions as presented by the patient today In view of the history and clinical findings, I should treat this patient for papulonecrotic tuberculid

DR SAMUEL AYRES JR, Los Angeles I felt the same way about this case The distribution of the lesions on the legs and arms predominates, and the eruption is worse during the cold weather It is better in the summer It strikes me that papulonecrotic tuberculid is the most probable diagnosis

In regard to the cases of mycosis fungoides I should like to say that I have been working with the A C S (antireticular cytotoxic serum) during the last year or so I have 1 patient who apparently has had a remission with the serum which was furnished by Dr Straus, of the Cedars of Lebanon Hospital The case was typical, microscopically and clinically, although not a far advanced one One case in which the serum failed was a far advanced case Another case apparently got out of control A C S serum, I think, is worthy of a trial, with little risk The results are not as dramatic as those reported with nitrogen mustard Dr Straus, pathologist at the Cedars of Lebanon Hospital, told me personally of a patient with lymphosarcoma who apparently recovered after A C S was

DR PAUL FASAL I agree with Dr Ostwald that this is a case of acrodermatitis chronica atrophicans The patient was born in Austria, a country where such cases seem to be much commoner than in this country A case of poikiloderma vasculare atrophicans of such long standing would resemble a roentgen dermatitis and not only show atrophy

A Case for Diagnosis (Periadenitis Mucosa Necrotica Recurrens?) Presented by DR ERVIN EPSTEIN, Oakland

A Case for Diagnosis (Pigmentation and Atrophy of the Face and Neck, Lupus Erythematosus?) Presented by DR H V ALLINGTON, Oakland

Localized Scleroderma Presented by DR ARNE E INGELS

A Case for Diagnosis (Angioma Serpiginosum?) Presented by DR H V ALLINGTON, Oakland

Sarcoidosis Presented by DR ERVIN EPSTEIN, Oakland

J C A, a 27 year old Negro, was first seen on Dec 16, 1946, because of an eruption on his face, neck, elbows, knees, perianal area and penis The condition started with parotitis in January 1943 This was followed by joint pains for which he was hospitalized in an Army hospital Investigation revealed roentgenologic evidence of enlargement of the mediastinal lymph nodes and parenchymal infiltration in the lungs The tuberculin reaction at this time was reported as "questionable" His electrocardiogram revealed inversion of the T wave in the first lead While he was in the hospital, generalized lymphadenopathy, cutaneous nodules and iridocyclitis developed Biopsy of a lymph node was said to have showed the histologic picture of sarcoid

When first seen, nearly four years after the first attack, he presented multiple discrete and coalescing nodules in the aforementioned locations The lesions were elevated, firm, nontender and in some instances umbilicated On the face particularly, the nodules were grouped around the eyes, nose and mouth Lesions were present on the nasal mucous membrane There was enlargement of the cervical, posterior cervical, supraclavicular, inguinal and axillary lymph nodes Corneal opacities were present

The biopsies from the skin and the lymph nodes showed epithelioid tubercles without caseation and occasional giant cells in the derma which were considered diagnostic of sarcoidosis

Numerous blood cell counts gave essentially normal findings Results of multiple urinalyses were normal Intradermal tuberculin tests elicited negative reactions to both the first and the second strengths Six Kahn tests gave positive reactions One Kolmer test gave a positive reaction, two were doubtful and one negative His wife is being treated for latent syphilis The total blood proteins were 6 9 mg per hundred cubic centimeters, the albumin being 2 72 mg and the globulin 4 18 mg Results of six blood calcium tests ranged from 12 to 14 mg per hundred cubic centimeters Nasal scrapings did not reveal acid-fast bacilli Roentgen studies revealed a few indefinite nodules in the upper lung fields and enlarged noncalcified nodes in both hili Roentgenograms of the hands, abdomen and lumbar vertebrae were normal Electrocardiograms showed diphasic and negative T waves in the four chest leads, indicating myocardial damage

1 1,000, 1 100 and 1 10 and undiluted tuberculin were all negative A roentgenogram of the chest showed moderate enlargement of the hilar lymph glands bilaterally Results of laboratory studies in 1945, including urinalysis, complete blood cell count, serologic reactions, and serum protein, were all essentially normal No skeletal lesions were found in 1945

The patient was seen in the Dermatology Clinic on May 13, 1947 Examination revealed multiple nodules and plaques on the face, extensor aspects of the arms and the left leg These lesions are firm and elastic to touch Many of the face lesions are depigmented The plaquelike lesions show a tendency toward central involution with a spreading border The lesions are dull brown to purplish Enlargement of the proximal phalanx of the third finger of the right hand was noted A roentgenogram of the hand showed widening of the base of this phalanx The medullary spaces are widened with intervening thin trabeculae The cortex is intact.

Treatment with vitamin D_2 (drisdol®), 150,000 units daily, was started on May 13, 1947 On May 16 she noted a flare-up of the cutaneous lesions with subjective throbbing sensations When seen on May 20, the flare-up had partially subsided, but some swelling was still noticeable

A biopsy specimen of a cutaneous lesion showed mild acanthosis of the epidermis The dermis contains a dense infiltrate consisting of lymphocytes, epithelioid cells and a few polymorphonuclear leukocytes In the deeper part of the corium there are well defined nests of infiltrate surrounded by connective tissue Vascular dilatation and some connective tissue degeneration are present

DISCUSSION

DR H E MICHELSON, Minneapolis I think that Negro patients having what is known as sarcoidosis should be observed in a most thorough manner to determine whether this uniform condition as seen in Negroes is the same as sarcoidosis in white persons, which might enable one to find out whether sarcoidosis is or becomes tuberculosis I have tried vitamin D_2 in 5 patients, with the dosage used in lupus vulgaris, and have seen no appreciable results

DR ARTHUR C CURTIS, Ann Arbor, Mich Although sarcoid is a clinical entity, I do not think that it is an etiologic one, unless one wishes to consider that perhaps a chemical compound is its cause This may be illustrated in the work originally done by Florence Sabin, when she began her work on fractionation of the tubercle bacilli She injected each fraction into animals, and sarcoid lesions developed in those receiving the phosphatide Further work has been done by others The late Dr Gardner, of Saranac Lake, insufflated animal lungs with silica dioxide and obtained typical sarcoid lesions Later Dr Allon in Toronto repeated Gardner's work and obtained the same results but noted considerable fat in the sections He then extracted these lungs with a solvent, removed the silica and reinjected the silica-free material into animals and again obtained sarcoid-like lesions This work indicates that silica may be an etiologic factor in sarcoid, silica produces the phosphatide which Sabin showed to be the chemical substance capable of producing sarcoid in animals

Not long ago a young man was seen with a typical sarcoid lesion of the face, proved by biopsy Dr Weller saw a few particles of silica in this lesion The next time I saw the patient I learned that two years previously he had been in an automobile accident and thrown out of his car, abrading his cheek on a gravel road I think that his sarcoid was due to silica ground into his cheek by the accident

Dr Michelson said that he has used vitamin D_2 without success That is not my experience The patients my co-workers and I have selected have had extensive

sarcoidosis, much as Dr Rothman presented today, where there was involvement of bone, lymph glands and skin We have studied the cases extensively by biopsy, chemical studies and roentgenogram In this series, to be presented before the Society of Investigative Dermatology, many showed striking improvement with vitamin D_2 and dihydrotachysterol therapy

DR STEPHEN ROTHMAN I agree with Dr Curtis that sarcoid structure has a multiple etiology, sarcoid leprosy, sarcoid syphilis and foreign-body sarcoids being important examples Still, there is a rather well defined entity of "sarcoidosis" with characteristic involvement of skin, bone, eyes and lungs, and evidence is accumulating that this disease is of tuberculous origin The "positive anergy" to tuberculin and the tuberculin-neutralizing properties of the blood serum are present in such high percentage in our material that it must be regarded as highly characteristic for this condition

DR ARTHUR C CURTIS I did not intend to leave the impression that sarcoidosis is not a clinical entity I think that it is Nor did I mean that silica or a foreign body reaction is a common cause of sarcoidosis There are some cases in which it may be the etiologic factor

Familial Keratosis Pilaris with Monilethrix-like Anomaly of the Hair in Fourth Generation, Maternal Side Presented by DR S ROTHMAN and (by invitation) DR R J STANWOOD

Dermatitis Herpetiformis Potentiated Effect of Pyribenzamine-Sulfapyridine Combination Presented by DR S ROTHMAN and (by invitation) DR J H MCCREARY

DISCUSSION

DR STEPHEN ROTHMAN In this case tripelennamine hydrochloride (pyribenzamine®) acts not because it is an antihistaminic drug, but because it contains the pyridine nucleus The therapeutic result in this case has been strikingly good

DR ZACHARY FELSHER (by invitation) There seems to be a relation, at least in some cases of dermatitis herpetiformis, between the presence of the pyridine group in the drug and its beneficial action In 2 of our cases of dermatitis herpetiformis both nicotinamide and pyridium® (phenylazo-alpha-diaminopyridine monohydrochloride) appeared beneficial Both drugs contain pyridine groups The disease in one of these cases was absolutely refractory to sulfapyridine, yet responded to nicotinamide and pyridium® In 2 other cases sulfapyridine caused complete clearing of the eruption, but nicotinamide and pyribenzamine® had no effect In a fifth case none of the pyridine-containing drugs worked at all I do not know the reasons for this discrepancy

In 1 of our cases of dermatitis herpetiformis which was completely controlled by sulfapyridine, 300 mg of paraaminobenzoic acid daily was given simultaneously to note whether this drug would interfere with the action of the sulfapyridine as it does in bacterial infections There was no interference with the beneficial action of the sulfapyridine Perhaps this points to the possibility that the action of sulfapyridine in dermatitis herpetiformis is different from its action in bacterial infections

DR ASHTON L WELSH, Cincinnati (by invitation) I did not see the patient under discussion, but I am interested in what has been said about the use of sulfapyridine in dermatitis herpetiformis In the last year my co-workers and I have treated a number of patients who had dermatitis herpetiformis with

Before examination the patient had received treatment, including roentgen and penicillin therapy According to the patient these did not improve the condition Since then he has received promin® (sodium p,-p'-diaminodiphenylsulfone-N,N' didextrose sulfonate) intravenously and locally, vitamin D by mouth, calcium by mouth and oxophenarsine hydrochloride intravenously The eruption has improved about 50 per cent in the past nine months Most of the improvement occurred while the patient was receiving intravenous injections of promin®

DISCUSSION

DR ROBERT C LOFGREN I agree with the diagnosis and might mention that at the Fort Miley Veterans Hospital I have seen 4 cases of sarcoidosis recently. One of these cases showed an unusual grouped follicular eruption Microscopic examination of one of these lesions showed the typical tuberculoid infiltration about the hair follicles and the sweat glands This type of eruption is not usually mentioned in the literature as one of the manifestations of sarcoidosis

DR ARNE E INGELS I must say that the case is extremely unusual clinically The lesions had lasted long enough to produce atrophy I have not seen destructive atrophy Second, I did not see the sections which were presented Third, I failed to see the report of roentgen examinations I think the case deserves further consideration

DR ERVIN EPSTEIN, Oakland Histologic sections were presented and represented classic examples of sarcoid in the skin and in the lymph nodes As far as the roentgen examinations are concerned, the bones and the gastrointestinal tract showed nothing unusual The patient had some enlarged mediastinal glands but no involvement of the parenchyma of the lungs He is about 50 per cent better than when first seen The patient seemed to respond better to promin® than to anything else that has been tried

Granuloma Inguinale Successfully Treated with Streptomycin Presented by DR PAUL FASAL

A Case of Osler's Disease with Hereditary Telangiectasis with Tumerous Hemangiomas Presented by DR ARNE E INGELS

Frederick G Novy Jr, M D, *President*
Frances M Keddie, M D, *Secretary-Treasurer*
Oct 17, 1947

A Case for Diagnosis (Folliculitis Ulerythematosa Reticulata?) Presented by DR A A SMALL for DR W M MEININGER

Generalized Xanthomatosis Presented by DR FRANK K HAIGHT, Oakland, Calif

Multiple Idiopathic Hemorrhagic Sarcoma of Kaposi? Stasis Dermatitis? Presented by DR ROBERT C LOFGREN

Dermatomyositis Presented by DR ERVIN EPSTEIN, Oakland, Calif

lowing 'What is your skin trying to say for you?" or "What is there of your inner self which is revealing itself through your skin?" or "What is your skin expressing?" or "What do you suppose your skin is acting out?" The physician has to be very comfortable with the idea that personal feelings and experiences will use body organs for expression Only when the physician believes that such things can happen and is personally comfortable in his own thinking about these concepts, can he bring the patient to make his contribution in treatment cooperation

NEUROPHYSIOLOGIC CONNECTIONS BETWEEN EMOTION AND SKIN DISEASE

Now it is unlikely that there is any symbolic expression of ideas or attitudes anywhere in the body which does not utilize nerve pathways, vascular changes, chemical alterations and structural tissue changes as the medium for transmitting the message In some cases the psychic stimulus acts over a short period and then wanes in strength or is neutralized by a counterphenomenon, as, for instance, the homesick man or woman who is able to return home In other cases the stimulus acts continuously over a prolonged period and is neutralized with difficulty or not at all

Having enumerated the emotions and in a general way indicated their mode of action, let us turn to the emotional states in which we encounter a linking of emotions and skin problems

NEUROTIC EXCORIATIONS

As knowledge of human emotional needs and how they are met increases the line of division between what is neurotic and what is psychotic becomes less important There is a pattern of wholesome development of personality and adaptation, and if this pattern is not approximated the many devious by-paths of attempted solution are almost legion In neurotic excoriations, for instance, the patient may already be suffering from delusions of parasitosis before the behavior which produces the excoriations begins Even if delusions are not present there is a strong need to disfigure, to suffer pain, to call attention to the self, to seek attention in a perverse way because the more healthy wholesome way was never discovered and firmly established early in life The wholesome pattern of training tends toward beauty, culture and the esthetic satisfaction of others This brings rewards of ego satisfaction, but if they are unknown to the patient and if he knows and seeks pity, shocked surprise, anxious concern or even revulsion and condemnation, he nevertheless accepts this reaction in others rather than being a complete nonentity in their eyes Most people cannot stand being ignored, and self-mutilation producing an unsightly skin,

A Case for Diagnosis (Parapsoriasis? Dermatitis Medicamentosa? Vitamin A Deficiency?) Presented by DR A A SMALL for DR O E L SCHMIDT, San Mateo, Calif

A Case for Diagnosis (Lupus Erythematosus? Senear-Usher Syndrome?) Presented by DR A A SMALL for DR W M MEININGER

A Case for Diagnosis (Xanthoma Sine Diabetes? Necrobiosis Lipoidica?) Presented by DR ARNE E INGELS

Two Cases of Epithelioma Adenoides Cysticum, in Mother and Daughter Presented by DR ARNE E INGELS

N M, the mother, is 79 years old She has tumors ranging in size from 0 5 cm up to 3 cm on her chin, face and back The tumors are light pink or red, firm to touch, embedded and not painful Many of them have a semitranslucent appearance None is ulcerated There are no café au lait spots The patient gives the impression of average intelligence The tumorous masses have been developing gradually since as far back as she can remember The patient has always been in excellent health

A biopsy, performed Oct 15, 1947, showed epithelioma adenoides cysticum

A B, the daughter, who is 15 years old, shows ill defined nodules densely studded on the midline of her face, nose and forehead and on her extremities Some of the nodules have a reddish pink appearance with a capillary design The great mass of them are colorless, firm and waxy in appearance The front of the right thigh shows a partly pedunculated tumor, vivid red and sensitive, but not inflamed

She has always been healthy, and her intelligence is about average

A biopsy, performed Oct 15, 1947, showed typical epithelioma adenoides cysticum

DISCUSSION

DR H V ALLINGTON, Oakland, Calif I thought both cases very remarkable I did not realize that nodules of the size that the older woman presented occurred in this disease

DR ERVIN EPSTEIN, Oakland, Calif The lesions are similar to those seen in tuberous sclerosis and adenoma sebaceum It is often brought out in discussions that these diseases are related

DR ARNE E INGELS The lesions are not unlike those of tuberous sclerosis, without the typical sclerosis The accepted name for the cutaneous lesions is epithelioma adenoides cysticum Sections which I expected to be ready were not I have seen cases in which microscopically the nerve elements were interspersed with the usual elements and collagen The very unusual tumor formation which you see in this case I have seen many times previously

A Case for Diagnosis (Leukemid? Purpura Urticans?) Presented by DR. A A SMALL for DR O E L SCHMIDT, San Mateo, Calif

E J, a 46 year old housewife, was well until June 1947, when she began to have weakness, soreness of her mouth and some purpuric spots on her extremities

like a social act of bravado, is preferable in certain egos to the emptiness of oblivion If delusions are present as the basis of self-inflicted excoriations which follow, we should, instead of speaking of the role of emotion in skin disorders, speak of the invasion of morbid ideas when healthy emotions and ideas are absent Happy people, i e , people with a sense of well-being, tend to seek out others and join in mutually pleasurable behavior It is when this sense of well-being is absent that an individual falls back on himself, feels himself, "tunes in on himself" to use the expression of one patient and falls prey to ideas of something morbid or unhealthy in his skin or some other part of the body

DERMATITIS FACTITIA

In dermatitis factitia we see the patient secretive about his goal He wants attention, but one must be a detective and guess he wants it He even tries out one's diagnostic acumen like the children in New York who recently ran away from home and hid in a cemetery and when found by detectives said "we just wanted to see if you were any good at your business" The patient with dermatitis factitia seems to enjoy challenging the physician to make a diagnosis for the pleasure of being enigmatic (to see if the physician knows the business of understanding people) before the real question of the motive of self-mutilation ever becomes an issue

EMOTIONS AND SKIN SENSITIVITY

Eczema There is increasing evidence that maternal rejection plays a large role in psychosomatic conditions, just as in neuroses and psychoses [1] In fact, we do not mean to distinguish between these three divisions of emotional conditions too sharply, for clinically they merge as different manifestations of the same basic emotional and ideational difficulties each merely having its own pattern and intensity This maternal rejection with its absence of affection to meet the minimum needs of love seems to leave the skin organ in a state of sensitive irritability or easy vulnerability to internal emotional conflict or external pressures or deprivations, just as the same conditions disturb heart action and normal function of the gastrointestinal tract or even prevent restful sleep Without the buffering or protective effect which a restful, secure relationship with the mother produces, we have a skin which might be subject to eczema or urticarial symptoms without there being an immunologic allergy in the patient [1] Miller and Baruch make a distinction between patients in whom asthma, hay fever, eczema and urticaria may have immunologic allergy as their source and those patients in whom

1 Miller, H , and Baruch, D D Psychosomatic Studies of Children with Allergic Manifestations, Psychosom Med **10** 275, 1948

In August 1947 she had severe vaginal bleeding which required six transfusions of blood Anemia, pronounced leukocytosis and early myeloid forms were noted in the peripheral blood

On entry to the Women's Medical Ward, Stanford University Hospitals, Aug 27, 1947, she felt well, mucous membranes were clear and pale, and the skin showed isolated red papules, 5 to 6 mm in diameter, with central pustules These red papules had an indurated base and were located on the right side of her neck, under the chin, in the right axilla and on the anterior aspects of both thighs, where some evidence of old ecchymoses was visible She had palpable inguinal nodes, a 1 cm firm node in the middle of the posterior cervical chain on the left and palpable supraclavicular and axillary nodes The edge of the liver was palpable 1 fingerbreadth below the right costal margin, the spleen was not felt She had vaginal bleeding At that time the red blood cells numbered 2,900,000, hemoglobin was 48 per cent, there were 54,000 white blood cells, with 30 per cent myeloblasts and 20 per cent myelocytes, and there were 81,000 platelets A sternal puncture showed many myeloblasts and myelocytes, with a few erythroid elements

On September 4, the uterus was packed with radium (2,400 milligram hours), and the vaginal bleeding stopped

By September 10, a severe gingivitis had developed, and the patient had a daily temperature spike to 40 C (104 F) By September 15, a large, tender, purplish indurated mass, 10 cm in diameter, had developed on the right buttock, at the site of the penicillin injections, and soon similar areas developed on the left buttock and on both arms where the patient had received injections of penicillin and morphine By September 22, the indurated, well marginated swellings on the right buttock and the right arm were covered with a brownish black crust, the patient had severe gingivitis, with a number of whitish, raised, circumscribed, necrotic lesions on the oral mucous membranes, and the liver and spleen were enlarged, as were the cervical, axillary and inguinal nodes

On October 7, the red blood cells numbered 900,000, the hemoglobin was 21 per cent and the white blood cells numbered 37,200, with 38 per cent myeloblasts By this time the black crust on the right buttock had come away, leaving a brown, indurated, well epithelized plaque underneath it The purplish areas on both arms had gradually become red at the center, and the advancing margins were still indurated and elevated about 7 mm above the surrounding skin These plaques were hot and pitted on pressure A biopsy specimen was taken from this lesion on October 10, with much oozing of edema fluid and blood, which was controlled with oxycel® gauze and pressure bandages

On October 11, the blood showed a definite shift toward older forms in the myeloid series The platelet count was 72,000 On the right forearm in the region of the elbow there developed a new raised, purplish, hot area which has been gradually spreading down the forearm the past week, until it is now about 10 by 12 cm There is some scaling of the older part of the lesion, and there the purple coloring is giving way to a pinkish hue The advancing margin is a slate gray, with numerous purple petechiae The mouth has gradually cleared of lesions The lesions on the arms, while still well marginated and tense, have become brown and nontender Her temperature has come down, and the patient is brighter

On October 15, the white blood cell count was 90,000, with an increasing percentage of mature forms, the packed cell volume was 16 mm , the bleeding time was 7½ minutes, and the clotting time (capillary tube), 2¼ minutes

Treatment has included administration of pentobarbital sodium, codeine, seconal,® acetylsalicylic acid, morphine and penicillin troches; injection of penicillin in oil

the symptoms may have nothing to do with immunologic allergy They feel that psychologic elements do not produce immunologic allergy but that in many patients similar symptoms may certainly not be the result of immunologic allergy Such patients who are not allergic in the immunologic sense would, we assume, have this sensitivity of skin in the same way that some patients have a most labile heart action, others have a sensitive stomach and others are sensitive sleepers We are especially indebted to Miller and Baruch for including in their study a control group of children Further studies of this kind with controls are much needed in this field of our mutual interest This would mean that when the child or the adult was under stress or when the relationship of the child and the mother or her substitute was endangered, the skin would be vulnerable to symptomatic reactions [2] Certainly, we observe frequently enough inflammation, itching and weeping of the skin in eczema when the patient is going through some environmental stress, which places him in a position of responsibility where he feels alone and unprotected Then he has a longing expressed in the skin by itching which calls for the soothing hand (The hand which scratches is the soothing hand, temporarily at least) He cannot weep, but his skin weeps for him Eczema patients are usually depressed and long for love, but they can't use love when they get it It may even tend to aggravate them They long to scratch instead, but they are only the more aggravated by scratching After all, love has been defined as "an itch one can't scratch" So far as itching may represent a desire for love, certainly scratching is an unsuccessful attempt to obtain it

PRURITUS ANI AND VULVAE

A later period of emotional fixation would be when in the course of psychosexual development, the potential pleasure for sexual excitement and orgasm never fully reached the genital region It remained in the anal region and scratching served the role of a sexual excitement, instead of the mature genital pleasure Pruritus ani and vulvae is not always psychologic in origin, but a psychologic factor doubtless plays a contributing role in many cases That this is true does not preclude some capacity for normal sexual function in the individual with the condition The case is not, in other words, one of a normal or a perverse way of sexual gratification, but it can include a little of both, and this should be investigated as a possibility in each case of pruritus More than one patient has said such things as the following about pruritus, "It's like being excited sexually, only one is never able to achieve an orgasm It's only excitement and tension and no let down"

2 Saul, L J Relations to Mother as Seen in Cases of Allergy, Nerv Child 5·332, 1946

and wax U S P, 300,000 units daily, from August 27 to 31, and of aqueous penicillin from September 9 to 20, administration of pyridoxine, and numerous blood transfusions At present cold packs are being placed on the tender plaque on her right forearm

Examination of the sections showed large primitive cells resembling large macrophages

DISCUSSION

DR REES B REES I should suggest ecchymosis of the type often seen in leukemia, although histologically there was no definite leukemic infiltration

DR HARRY J TEMPLETON, Oakland, Calif The diagnosis, I think, is very clear There is leukemia with hemorrhage into the skin I should like to discuss this case from the standpoint of a possibly valuable new therapy, helpful to my associates and me in a single case A couple of years ago there was referred to us in Oakland a patient with chronic myelogenous leukemia, the diagnosis was proved by an internist and a hematologist Blood counts going back a number of years showed that the case was a rather typical one Generalized erythematous dermatitis, which became extremely severe, developed The patient had had about every type of orthodox therapy, without benefit I had read an abstract at about that time in which colchicine had been pointed out as having something to do with the cell mitosis It is used by planters for treatment of seeds of plants and seedlings of plants, whereupon certain changes result in the production of entirely new varieties of the plants

We gave this patient colchicine, 1/100 grain (0 5 mg) tablets, every three to four hours to the point of tolerance, that is, until the patient got nausea, abdominal cramps and diarrhea At that time the dosage was dropped to one or more tablets a day, the number depending on how well the drug was tolerated The cutaneous lesions began to improve and then disappeared after the patient had taken colchicine for two months About two weeks ago, at my request, Dr Paul Michael rechecked the blood count He stated that the man still had the hematologic picture of myelogenous leukemia, but that something had happened, there was a decided improvement in the blood picture, with less immature cells and more approach to maturity in the cells

Drs Lunsford, Allington and I have been seeking more cases of that sort Through the kindness of Dr Torrey several patients showing lesions of the lymphoblastoma group have been started on colchicine treatment at the University of California Clinic

DR FRANCES A TORREY At the present time I do not feel that my associates and I have anything definite to report We have 3 cases diagnosed as mycosis fungoides One of them we have been following for a long time Biopsy of the skin in each confirmed the diagnosis The patients in 2 cases have been able to tolerate colchicine in a dosage of 1/100 grains three times a day But so far there has been no definite improvement However, because of the characteristics of the disease, I think it is too soon to give a report

DR HARRY J TEMPLETON, Oakland, Calif At my request Dr Leslie Smith of El Paso, Texas, started treating a patient with a lymphoblastoma with colchicine This patient responded dramatically at first, and then the condition apparently flared up The dose was increased, and I am waiting to hear Dr Smith's report of the outcome

DR JAMES R DRAKE I should like to ask Dr Templeton whether he is interested in using colchicine in treatment of other diseases of the lymphoblastoma group

DR HARRY J TEMPLETON, Oakland, Calif Yes

CANCER PHOBIA AND SYPHILOPHOBIA

These conditions are not actually cutaneous conditions but psychiatric conditions and severe ones at that, but since their nature is such as to bring them to the attention of dermatologists, some discussion of them seems pertinent in a paper of this kind Just as maternal rejection may sensitize the skin to minor or major departures from peaceful and quiet functioning, so the same state of affairs prevents an emotional buffering from morbidness of mood When a person feels unloved and does not have the interest of those who have power and wish to protect with that power, ideas spring up in the mind of destructive forces invading the organism In childhood it is the bogeyman or wild animals, while in adulthood it is the undue suspicion of burglars and violence or of invasive cancer or syphilis Syphilis or cancer is merely the later life formulation of the bogeyman or the wild animals In either case, pain, destruction of tissues and eventual annihilation are felt to be the end result In phobias there is a great distrust born of real events in early life which would normally evoke distrust There are guilt and feelings of unworthiness There is great difficulty, amounting to almost complete inability in some cases, to trust and believe in the one who would help them Out of a long-carried-over feeling of guilt they think, "I should be the victim of a destructive disease I deserve no better fate Something dreadful must happen to me to even the score I am being, or I will be, punished for my wicked thoughts and acts" In therapy the task is to have the patient feel a warmth toward others and a joy in doing for others, so that he begins to reestablish a feeling of worthiness This must provide the ground work for interpretation of the symptoms No belief in a worried person is senseless Every belief has a cause in some earlier experience There is not necessarily one thought or fantasy which, if discovered, enables the whole neurosis suddenly to disappear This happens only rarely In these cases most of the results depend on slowly enriching the empty emotional life, which has left room for morbid ideas, and coming to an understanding of why a painful thought like that of having cancer or syphilis can serve any purpose It serves to atone for some childhood misdeed or "bad thought" Only when this is understood and the patient can forgive himself, can he understand how to have a life free of the burden of constant preoccupation with such distressing thoughts Some of these patients improve and get well with a few psychotherapeutic interviews—three to six in number Most of them, however, if their disease is of more than six months' duration, need longer, more intensive psychiatric treatment and should be referred to a psychiatrist for treatment if feasible These cases can be among the most difficult in the field of psychiatry

Archives of Dermatology and Syphilology

VOLUME 60 DECEMBER 1949 NUMBER 6

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ROLE OF EMOTION IN DISORDERS OF THE SKIN

O SPURGEON ENGLISH, M D
PHILADELPHIA

WHAT emotion plays a role in disorders of the skin is a fact accepted by most, if not all, dermatologists This fact has been well elaborated in the literature, both by those specializing in the field of dermatology and those in the field of psychiatry who have joined with dermatologists in thinking through some of the complicated disease conditions within that field of endeavor

The psychosomatic approach to any disease makes a much greater demand for knowledge of causes, pathologic processes and procedures of treatment than any single newly discovered disease This is because a whole new system of dynamic forces, emanating from the mind, which act as toxic agents, must be known and understood Emotions can be helpful phenomena in the life of man, but they can also be harmful and make him sick These emotions must be understood as causes of symptoms, with some ability on the part of the physician to assess and weigh them quantitatively It must be known what kind of pathologic changes they will produce and also how therapeutic manipulation of these emotions will cause them to lose their capacity for producing end results of disease in the skin Before passing to the role of emotions generally and what they can do, let us see what the commoner emotions are which are prone to be causes The most commonly encountered emotions are the following

1 Need for love (approval, appreciation, recognition)
2 Anxiety (fear and worry)
3 Hostility (anger, hate, aggression)
4 Inferiority feelings
5 Ambivalence
6 Guilt
7 Ambition (competition)
8 Envy

NEED FOR LOVE

The need of love is one of humanity's greatest hungers, and many other emotions are dependent on it From the cradle to the grave human beings struggle under it Some of them have a great hunger for love

From the Department of Psychiatry, Temple University School of Medicine

TRICHOTILLOMANIA

Trichotillomania is likewise not really a condition of the skin but a piece of neurotic behavior What one sees in the hairy regions are the end results of a compulsion to extract the hairs forcibly with the fingers or other means This unusual behavior starts as a perverse means of gratification, of producing, in other words, pleasurable pain Those whose behavior is of this sort are in the class of those who bite and pick the nails until the nails are painful and bleeding, crack their finger joints, stimulate the gums with toothpicks or other instruments until the gums bleed or who squeeze and press comedos until they have produced macerated areas and bruises Tugging at ear lobes, biting the lips or pinching the skin are other manifestations of efforts to produce a pleasure-pain effect on the body, because more natural and wholesome ways of relieving tension either have not been permitted or have not been taught early in life They play with themselves, stimulate themselves and usually disfigure themselves, mainly because the activity gratifies This fact is hard for average people to understand, but it is no more enigmatic than the fact that people consistently eat or drink more than is good for them In either case they (1) indulge themselves in something they enjoy, (2) they relieve tension at the moment, (3) they put themselves at a disadvantage in the eyes of others through it but (4) there is an insistent urge to repeat it for the momentary pleasure it produces From this description its sexual component can be seen To cure it, the physician has (1) to help the patient to endure the tension on cessation of the habit and (2) to get the energies channeled into more wholesome and useful directions

HYPERHIDROSIS

Excessive sweating of the hands, axillas and feet is fairly common. It probably could not be settled at the present time whether there is any inherent pathologic condition of the sweating mechanism or whether this manifestation is entirely emotionally conditioned There is considerable evidence for the latter There seems every reason to believe that the sweat gland mechanism might have as wide variation in function as the glands in the mucous membrane systems of the stomach, the intestine and the respiratory and genitourinary tracts One must grant that there is wide variation in the outpouring of secretion in these areas, and the skin response could be just as labile We see analogies in sphincter control, where in states of fear people cannot "hold their water," and it drips from the hands, axillas and feet and often other parts of the body as well Whether there is any wisdom of the body in this mechanism, that is, whether there are any conditions under which

but either have no recognition of what they need or have no technics for obtaining it Lack of it brings such untoward emotions as frustration, hurt pride, envy and jealousy Others have perverted and symbolic ways of obtaining it through excessive use of alcohol, food, sex or drugs Others know they need affection, attention and rewards, and they take the conventional kind of actions and responsibilities which bring them the love they need and its derivatives of approval, appreciation and recognition Thus, to be assured of love is a most important emotional need and sufficient gratification of this need is of the greatest importance to health, both physical and mental

There has been a general reluctance to accept the proposition that love is an actual necessity for health and happiness As a health factor it has not had the same scientific standing as the chemical symbol for iron, for example, but the more one studies man and his various illnesses, the clearer it becomes that he can live neither a healthy nor a wholesome life without it

ANXIFTY

Anxiety is one of the earliest emotions aroused and one of the most basic in the whole life of man Fear is its conscious representative but the origins of anxiety itself are largely unconscious We have to use the word "fear" in order to describe the origins, since anxiety arises predominantly out of two early life situations, namely, fear of physical harm, pain or injury and fear of the loss of love When the child is threatened with the loss of his mother's protective presence, he sustains uncomfortable sensations, in both the mind and the body, and in describing his reaction to this situation we say he fears a loss of love (meaning the loss of a friendly presence) Also, as the child comes to suffer pain from falls, bumps, rejection or punishment, he dreads its repetition Its possibilities of repetition fill him with the same uncomfortable sensation, and we call this sensation anxiety Anxiety has two components one of them being psychic and distressing to the mind in a varying degree The other, the somatic component, arises from the fact that once the distress of the psyche has reached the threshold of action the emotional energy overflows by way of the autonomic nervous system to any or all parts of the body People who in the ordinary course of life suffer from too much anxiety are people who in early life lacked a consistent supply of a reassuring, friendly presence or who were subjected to too many real pain-inflicting experiences or threats of them This allows a dread or a worry pattern to construct itself, and as life becomes more complex the things which threaten deprivation of love and security or real physical distress increase in number

Not only does the emotion of anxiety impair one's ability to enjoy life, but it has more far-reaching effects If one's energy is used up in

this would be advantageous is unknown to us MacKenna[3] suggested that "a patient suffering from pompholyx may be indicating by a psychological mechanism that he cannot use his hands and feet" However, in psychiatry, when hyperhidrosis is an accidental symptom of an otherwise more inclusive neurotic pattern, we frequently find that in the course of gaining the security which cures the other symptoms, hyperhidrosis ceases In this connection, Wittkower,[4] in a study of 50 patients with pompholyx, found them to be unusually narcissistic, and four-fifths of them had shown other outstanding neurotic symptoms prior to or at the time of onset of the condition He found them vain and affected in their manners and speech They were ambitious but afraid of failure They were afraid of getting hurt physically and emotionally They were afraid of exposing their own feelings to others If severe hyperhidrosis exists alone as the main complaint and is unresponsive to local treatment, psychotherapy should surely be utilized As in blushing or more particularly the fear of blushing (erythrophobia), the patient may be reluctant to spend the time necessary to get at the emotional basis of a symptom which appears simple in nature but actually has a great deal of psychopathologic material underlying it Should the patient decide to undergo intensive psychotherapy for a symptom like pompholyx or erythrophobia, there is no question but that his personality would derive great benefit as a result of the changes he would have to make to get rid of his symptom The patients rarely realize that they need to get any help with their personality, generally feeling adequate in this area However, in making this need clear to the patient we may help him to decide that the treatment for the removal of just one symptom, which at first glance looks tedious and expensive, should be undertaken Just one such symptom may render a patient ineffectual and miserable, so the fact that the treatment offers two benefits may be the means of getting him to accept and participate in the therapeutic program

URTICARIA

Urticaria is one of the conditions of the skin for which an emotional factor has been noted and accepted for some time As yet it becomes difficult to specify the emotional trends which, among other factors, enter into this condition Stokes, Kulchar and Pillsbury[5] concluded

3 MacKenna, A M B Psychosomatic Factors in Cutaneous Disease, Lancet **2** 679, 1944

4 Wittkower, E Psychological Aspects of Skin Disease, Bull Menninger Clin **11** 148, 1947

5 Stokes, J H , Kulchar, G V , and Pillsbury, D M Effect on the Skin of Emotional and Nervous States Etiological Background of the Urticaria with Special Reference to the Psychoneurogenous Factor, Arch Dermat & Syph **31** 470 (April) 1935

concentrating on the feared thing, in the hope that by this wariness it can be averted, too little energy is left for happy living If this phenomenon goes on long enough and severely enough, the body can no longer function properly and symptoms of illness have arrived These come through the mechanism I have already described, by which emotional energy is converted into somatic disturbances through the autonomic nervous system We then have psychosomatic symptoms

HOSTILITY

Like the need of love, hostility is also ubiquitous Without spending too much time on the philosophic theories of the origin of hostility, let us say simply that when the human organism fails to find conditions which keep him in a constant state of well-being, he experiences an unpleasant emotion accompanied by ideas of retaliation and the use of force to gain his ends, even of destruction of the person or thing which makes him uncomfortable or which thwarts him This we call hostility It is impossible to conceive of any one in our society without any hostility whatever, but certainly small amounts can be present without too many untoward results This is true, especially if the modicum is properly blended with the rest of the personality to produce wit or zestful, spicy conversation or if it results in a wholesome competition "Get up and git," or "I'll show them," is an aggressive philosophy, which contributes to progress individually and generally But, unfortunately for society, a great deal of hostility does not take this form It does not even find vent in occasional outbursts of anger, righteous or otherwise It has to be held in check, because the child or the adolescent does not feel that his environment will tolerate any show of hostility He fears rejection or punishment, so his holding in results in repression a "burying alive" process of which the mind is capable The buried or repressed hostile activity builds up, and the more it builds up, the more labor another part of the mind has to exert to keep it from breaking out While this battle is going on there is much less energy available for friendly relations in other directions In fact, the person having this internal struggle becomes guilty about his state and not only feels no impulse toward loving but thinks that he does not deserve to be loved The results of this continual psychopathologic engrossment may be various things, one example being the obsessive thought that he will harm somebody However, we are more interested in where the hostile activity that builds up within expresses itself somatically We discover that it goes in several directions to produce disturbances of the upper and lower gastrointestinal tract and enuresis, headache, ticlike movement, probably epilepsy and disorders of the skin, and plays a role in vascular hypertension and other disorders Actually the effects of these

from a study of 100 cases that the patients were of the driving, high tension, competitive type, keyed to high pitch and perpetually intent on a destination to be achieved at no matter what expense Saul [6] seemed to find that longings for love frustrated through fears of sex in persons with a highly erotized skin were responsible for attacks Both observations have the common denominator of intense longings for achievement of gratification If we keep in mind that there are many hard-driving people who long for things without getting urticaria, but that it is this type of personality which furnishes the final factor that sets the symptom complex into motion, and that this factor can be treated and tension in this direction lowered, we have done the most fruitful thing possible toward relief of the symptoms

SEBORRHEIC DERMATITIS

Ingram [7] in 1939 called attention to the emotional instability of those suffering from seborrheic dermatitis by stating that it could vary from the sullen, sulky indolence of patients who present some of the heavier forms of acne to the high-strung overactivity of the patient with rosacea "States of anxiety, stress, and strain are conditions which the seborrhoeic will not readily tolerate" Ingram studied 100 seborrheic patients and found them hard to study, as they were not easy talkers and were afraid of persons in authority They were shy and solitary and had trouble in social contacts When with people they felt lost, exposed, uneasy and tongue-tied They could not stand hostility toward themselves They were compulsive workers and perfectionistic They were sensitive and felt inadequate As might be expected from such traits, they were unaggressive and overcompliant No follow-up treatment is reported, but it could be assumed that any cutaneous symptom present with such marked disturbances of personality should improve under effective therapy

The same author studied patients with psoriasis and found no specific type of personality, but concluded that the proportion who were maladjusted was far in excess of the proportion of such persons in the general population

As the role of emotions in cutaneous conditions becomes more widely accepted, we shall have more psychotherapeutic efforts and hence more reports of results of treatment This will be good for the morale of both dermatologists and patients alike As things stand, the patient still has too little faith in what can be done for his condition by a psychotherapeutic approach It is really hard for him to look at his emotions,

6 Saul, S J, and Bernstein, C The Emotional Settings of Some Attacks of Urticaria, Psychosom Med **3** 349, 1941

7 Ingram, J T The Seborrhoeic Diathesis, Brit M J **2** 5, 1939

forces of which people individually appear so unconscious have long since been noted by them in general in that they observed that situations gave them "headaches" or "made them sick," or they "itched for a fight" and "got their blood pressure up" over something frustrating Since people are not proud about being irritable, disagreeable, unpleasantly aggressive, arrogant, demanding, tyrannical or domineering, they remain remarkably unconscious of the hostile motivation But there are tremendous quantities of hostility latent in the human race, producing not only serious social problems but many individual symptoms of illness as well

INFERIORITY FEELINGS

To many it might appear that feelings of inferiority could exist as a social phenomenon but not one with any medical implications But feelings of inferiority are closely linked up with the basic emotions of love and hate Obviously, the person having feelings of inferiority has not had enough acceptance and appreciation There are few people who ever feel quite satisfied with themselves, but in some persons the feeling of worthlessness can be so deep as to destroy the capacity of the psychic apparatus for maintaining physiologic equilibrium Once a feeling of inferiority is deeply set, it is not easy to restore the self-esteem to a proper balance

AMBIVALENCE

"Ambivalence" is a term given to the condition of directing both love and hate toward a person or the world in general These impulses may be present practically continuously and show themselves rather subtly, or they may show themselves more superficially and plainly by a capricious change of mood and attitude, in which those associated with them are loved one hour or one day and hated and condemned the next We see a man, for instance, who protests how much he loves his wife but never listens to her requests, her suggestions, never tries to further her plans and never helps her in any tangible way We see a woman who protests that she loves her child but who never allows the child to do anything he enjoys and never lets him decide anything for himself This mixture of emotions which has the descriptive term of ambivalence, which portrays it as one emotion, can, like guilt, block off the benefits of straightforward, friendly, satisfying and wholesome human relations

GUILT

Guilt is an emotional distress resulting from criticisms voiced by the conscience, the conscience being a well preserved memory pattern of what the parents or substitute mentors said was right and proper The person undergoing guilt has reason to feel that he has not been or is not

since he is too busy looking at his skin and sees little reason why he should shift his attention to his emotions, which he considers as secondary to the state of his skin But as word gets around that one's disposition can be expressing itself in the skin, the physician can obtain more cooperation in the psychotherapeutic treatment

The emotional factor is a variable one, and no one is trying to assert that skin diseases are due to emotions alone But when emotion is a factor, it is one that must be dealt with, if well dealt with, it may be the factor which will give the most practical results in comfort and hence in satisfaction to both patient and physician Dermatologists and psychiatrists must stimulate and help each other to carry on more therapy of the emotional forces which are using the skin for their expression Psychotherapy is not a simple, easily mastered tool, and the patient is not always a willing subject for therapy But, if we try to ascertain what the role of emotions can be in conditions of the skin, we will cure the condition in occasional subjects, improve it in some, make it easier to live with in others and find the specialty of dermatology altogether more interesting through the pleasure which comes from taking a greater interest in human emotions in our daily work as physicians

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living up to expectations This emotion can kill the joy of living and may cause the patient to adopt a life of excessive self-sacrifice, which in the course of time produces physiologic disturbances As an emotion it acts to block the reception of impulses emanating from others of love and approval Starvation of the love needs can occur from guilt and the pathophysiologic results in the way described earlier

AMBITION (ENVY, COMPETITION)

The ambitious person does not necessarily have pathologic emotions, but he certainly runs the risk of being infected with envy or excessive competitiveness These emotions tend to produce tension, and the professional, financial and social success of many people has been paid for at a high price, i e., the price of tension, which is prone to express itself through the nervous system on many parts of the body The aggressive component inherent in these emotions plays a large role in such conditions as cardiovascular disease, migraine and vascular hypertension, and to some degree in many others A successful person can have achieved his goal by great ability and a friendly, easy-going manner, but he is *in the minority* Ambition with its attitude of competition, sometimes accompanied by envy, is all too often carried along as unnecessary equipment on the road to successful service

With this section I conclude these brief pictures of the more common and important emotions which are going to affect the skin, if emotion is playing any role whatever

HOW THE EMOTIONS AFFECT THE SKIN

Since emotions will find expression in any or all parts of the body, it is inevitable that so important an organ as the skin should be affected Probably the greatest number of ideas relating to man's actions and feelings are spoken of in reference to the heart The stomach and bowel run the heart a close second, but the skin will not be too far down the list When, for instance, a man does anything free of blameworthy motives, we allude to him as acting "with a whole skin" When we escape injury, we "save our skin" Cheating or taking advantage of the other fellow is to "skin" him To be oversensitive is to be "thin-skinned" and to be relatively impervious to the attitudes of others is to be "thick-skinned" The expression "you are a scab" or "you give me the itch" are well known and indicate the response of the skin to hostility "I blush for you" means "I identify myself with you and disapprove of you" Such expressions indicate that the skin is a potent carrier of emotions and attitudes Just as the stomach may act in a perverted way when the personality is unable to cope with a problem, so the skin may do the same Our first impression was that emotion was slower to appear in the skin than in the heart or the gastrointestinal tract, but

OLD DERMATOLOGIC DRUGS WHICH SHOULD BE RETAINED

MARCUS RAYNER CARO, M D.
CHICAGO

WE ARE living in the "Golden Age" of dermatologic therapy, or so it would seem During the decade since sulfanilamide was first introduced into therapy a procession of new potent drugs has been added to our weapons against disease With the sulfonamide compounds in all their many variations, with penicillin, streptomycin, tyrothricin, bacitracin, aureomycin and other antibiotics yet to be named, with the vitamins in all their fractionations, with radioactive isotopes, and with the host of antihistaminic drugs it would seem that the therapeutic progress in these few years is unmatched in any period in history Only time and the merciless inroads of experience will tell whether these contributions will live through the ages as permanent achievements, as have the artistic wonders of the "Golden Age of Pericles"

It is unfortunate that all these drugs have appeared on the scene as "wonder drugs" Such an introductory appraisal is not conducive to the competitive emergence of a drug of permanent value Each drug was wishfully accepted as a miracle and at once was utilized in every conceivable disease It was only after mishaps, complications and failures that the faith in miracles was shaken and was replaced by the cold, analytic scrutiny that should be the challenge of all new drugs. There is much evidence already on record that not all the advances made by the use of these new drugs are permanent steps forward In the problem of infectious diseases there is a continuous adaptation of the micro-organisms, which in time prevents their complete annihilation Many of these drugs produce sensitizations or other toxic reactions which make their continued use hazardous It is true that all the new drugs are being constantly developed and improved While improvement is always a sign of progress, it is nevertheless also an indication that there are deficiencies that need correction

In times like these, when to the casual observer we dermatologists seem to be moving from success to success, it is well for us to look backward, to appraise the past and to hold fast to what is good In

Read at the Seventh Annual Meeting of the American Academy of Dermatology and Syphilology, Chicago, Dec 9, 1948

in blushing and sweating we have very prompt phenomena which sometimes are distressing to a repressive patient Also, urticaria and allergic phenomena have a high incidence and can make their appearance quickly Hence, so far as these two phenomena often have a large emotional component, we cannot say that the skin differs from other organs because it does not respond promptly Dermatology and psychiatry share the phenomenon of having a few acute conditions and many which are slow to improve Now the skin undoubtedly is like other organs in that it may symbolically represent an inner attitude In other words, the skin may give one away The well known phenomenon of blushing embarrassment indicates "I believe you know what I'm thinking and I'm afraid and ashamed" The blush symbolizes inner excitement with fear of exposure being prominent, the exhibitionistic wish, however, triumphs over fear and shame, which would try to keep these emotions hidden

But the skin, in addition to "burning" with shame, may weep out of sadness So just as there may be an idea quickly speaking its message by way of the skin, so long-continued tensions make themselves known through activity of the autonomic nervous system In adolescence, for instance, there are many conflicting feelings of being good and bad, of being attractive and ugly, of being clean and dirty, of being intelligent and stupid, all at the same time The restless longing for attention makes them latently strongly exhibitionistic It is a paradox that at the time they wish to be most presentable, attractive, lovable, beautiful, they are affected with acne or some other disturbance of the skin But if we grant that emotions affect the function of the skin at all, then it becomes plausible that they must show their worst side through disease of the skin Both children and adults may expose their worst behavior in a bid for attention The skin may take over this action What we must keep trying to do if we are to be successful in understanding the language of psychosomatic disease is to remember that the skin can act a certain way or act out a problem, just as the whole person may act through voluntary muscle activity

Since most physicians pride themselves on being practical men, these ideas may sound impractical and fantastic to many However, the practice of psychosomatic medicine requires that the physician use other aspects of his education than physics and chemistry It requires that he (1) utilize what he knows or can learn from the poet, the story writer, the artist and the philosopher and (2) bring this knowledge to bear on his patient's approach to the symptoms in question This approach seems less reliable and is certainly less tangible than remedies which can be taken internally, intravenously, intradermally, intramuscularly or by unguentation It takes a great deal of understanding and self-confidence to ask the patient some such question as the fol-

former generations, when nothing was known of the causes of most diseases of the skin, an attempt was made to treat the conditions symptomatically Because of the surface location of cutaneous lesions it was possible for physicians to experiment widely with all possible local medications and, by trial and error over the years, to develop topical therapy that was effective Much of accepted dermatologic therapy is based on this tediously developed but long-established foundation

In modern times, when very little more is known about the causes of most diseases of the skin, the emphasis has been placed on etiology The goal set has been to achieve specific treatment pointed to correcting definite etiologic factors This orientation may in time result in a brilliant solution of many of the baffling dermatologic problems There is the drawback, however, that we may for too long be withholding relief of symptoms and even possible cure by so-called shotgun therapy while we spend precious time in taking careful aim with a precision rifle—a weapon that in many instances may not even be loaded

It has been my impression that with the frequent addition of well publicized new drugs to the dermatologic armamentarium, many old ones have undeservedly been pushed into the background of daily thinking Dermatologists now being trained are often unfamiliar with old drugs that still have merit, and they tend to rely more and more on therapeutic weapons that may prove to be ephemeral With the purpose of emphasizing those drugs that have proved to be effective over the years in the work of successful practitioners, I addressed a letter to two hundred dermatologists of experience, asking them to list drugs of long-established usage that they still prescribe Replies were received from nearly all Most of those questioned were generous in listing the drugs they use most often in their work One dermatologist referred me to the "Pharmacopoeia of the United States" (U S P) and the "National Formulary" (N F) for drugs that still have merit I heartily agree that one may practice in our specialty very competently while limiting himself to drugs listed in those two authoritative books It is, nevertheless, true that in our Academy there are many who do not have in their offices, available for easy reference, the latest edition of either work, nor even that excellent small book, the "Epitome of the Pharmacopoeia of the United States and the National Formulary" I am glad to pass on the suggestion, however, and to recommend the "Epitome," always in the latest edition, as a book that should be accessible on every dermatologist's desk A careful study of its contents is rewarding in calling to attention many official preparations, easily compounded and readily obtained, that are useful in the treatment of many dermatoses Most of these preparations have the added virtue of being relatively inexpensive

sulfapyridine Several interesting observations have been made Apparently large amounts of sulfapyridine are usually unnecessary to control the reaction if pyribenzamine® is given simultaneously The 4 to 7 tablets of sulfapyridine daily can often be reduced to 1 tablet a day if pyribenzamine® is given at the same time It was our experience that pyribenzamine® alone has not been very helpful It has not been helpful in preventing the outcropping of skin lesions Another group of 10 patients who had dermatitis herpetiformis were treated with sulfapyridine and paraaminobenzoic acid simultaneously They were given as much as 100 mg of paraaminobenzoic acid daily We observed in only 2 of these 10 patients some inhibition of the action of the sulfapyridine In the other 8 there was no apparent inhibition of this action It appears that in dermatitis herpetiformis sulfapyridine has some action on the causative bacteria which is different from the action usually attributed to this drug on the bacteria involved in other diseases The paraaminobenzoic acid alone may have some favorable action in dermatitis herpetiformis, but to date we have not treated patients who had dermatitis herpetiformis with this drug alone This should and will be done to control the study already mentioned Suggesting some unusual action of the sulfapyridine on the bacteria in dermatitis herpetiformis is the fact that in many instances only 1 tablet daily, or 1 every other day, was necessary to control this problem This has not been an observation with this drug in other diseases

DR. ADOLPH ROSTENBERG JR (by invitation) I could not make a diagnosis of dermatitis herpetiformis In order to evaluate the therapeutic result one should be sure of the diagnosis I do not know that it was a papular eczema It started eight years ago

DR STEPHEN ROTHMAN Many of the outstanding New York dermatologists who saw this patient did not diagnose dermatitis herpetiformis because the patient displayed no vesicles However, after we had done a patch test with potassium iodide, the patient had a rather characteristic vesicular eruption Dr O'Leary saw the patient at that time and agreed with the diagnosis of dermatitis herpetiformis A few characteristic grouped vesicular lesions are still present

Kaposi's Sarcoma in a 50 Year Old White Man with Tumors on the Toes Presented by DR EDWARD A OLIVER and Dermatology Staff

A Case for Diagnosis (Exfoliative Dermatitis or Pityriasis Rubra Pilaris?) Presented by DR JULIUS E GINSBURG and (by invitation) DR I EIRINBERG

A Case for Diagnosis (Glossy Skin? Morvan's Disease? Possible Radio Dermatitis?) Presented by DR JAMES HERBERT MITCHELL and (by invitation) DR ROBERT H HARRIS

Generalized Mycosis Fungoides of Six Years' Duration Presented by DR EDWARD A OLIVER and Dermatology Staff

Acrodermatitis Chronica Atrophicans Presented by DR I M FELSHER and DR A SLEPYAN and (by invitation) DR I EIRINBERG

Alopecia Areata Totalis Associated with Hypothyroidism, Regrowth of Hairs Presented by DR S ROTHMAN and (by invitation) DR Z FELSHER and DR L RUBIN

Acrodermatitis Chronicus Atrophicans Presented by DR JAMES HERBERT MITCHELL and (by invitation) DR ROBERT H HARRIS

A Case for Diagnosis (Sarcoid? Syphilis?) Presented by DR EDWIN M SMITH JR

Supernumerary Breasts in Axillas (with a Nipple [?] on One Only) Presented by DR I M FELSHER and DR A SLEPYAN and (by invitation) DR I EIRINBERG

Von Recklinghausen's Disease (Neurofibromatosis) Presented by DR FRANCIS E SENEAR and Staff

Prurigo Nodularis Presented (by invitation) by DR ROBERT C RANQUIST

Erythema Induratum and Papulonecrotic Tuberculid Presented by DR MICHAEL H EBERT and (by invitation) DR ALLEN S PEARL JR

A Case for Diagnosis (Leprosy?) Presented by DR EDWARD A OLIVER and DR SAMUEL M BLUEFARB

Lichen Planus with Atypical Microscopic Picture? Lichenoid Toxic Eruption Presented by DR STEPHEN ROTHMAN and (by invitation) DR R H SNAPP

Erythema Figurata Perstans or Tinea Superficialis Squamosa Presented (by invitation) by DR MAURICE OPPENHEIM and DR WILLIAM A YACULLO

Parapsoriasis en Plaques Limited to Flexural Areas Presented by DR EDWARD A OLIVER and Dermatology Staff

A Case for Diagnosis (Glossitis Rhombica Mediana of the Brocq-Pautrier Type?) Presented by DR JAMES R WEBSTER

A Case for Diagnosis (Parapsoriasis en Plaques? Premycotic Mycosis Fungoides?) Presented by DR RALPH H SCULL

A Case for Diagnosis (Pemphigus?) Presented by DR D V OMENS and (by invitation) DR HAROLD D OMENS and DR J GRAFFIN

Chronic Discoid Lupus Erythematosus—Persistent Despite Treatment for Thirty-Four Years Presented by DR JAMES R WEBSTER, DR SAMUEL BLUEFARB and (by invitation) DR J GRAFFIN

Scleroderma Presented by DR DAVID V OMENS and (by invitation) DR B YAFFE and DR HAROLD D OMENS

A Case for Diagnosis (Granuloma Telangiectaticum?) Presented by DR THEODORE CORNBLEET and (by invitation) DR H SCHORR and DR B YAFFE

Nearly every dermatologist of experience has his pet remedy for each dermatosis, a drug tested by time and countless usages and at times inherited from his preceptor While the use of some of these remedies may represent wishful thinking and unwarranted enthusiasm, often it represents the product of careful observation of cause and effect by good clinical observers, whose experience should not be lightly brushed aside In the practical management of a dermatologic patient it is helpful for us to keep all these remedies in mind Far too often we dermatologists exhaust all methods of treatment which are indicated on rational grounds and in the end come up against the stark fact that our patient has not been helped at all It is helpful at such a time to be reminded of drugs that empirically and often without logical justification may succeed in giving the patient at least symptomatic relief

DRUGS FOR INTERNAL USE

Of the drugs used internally arsenic compounds probably have the oldest history and the most varied career from generation to generation Centuries ago they were used as a remedy for asthma For many years they fell into disuse medically because of frequent employment as a poison In the seventeenth and eighteenth centuries they were used medicinally only by quacks for treating fever and ague One of these quack preparations was so successful that a Dr Fowler had it analyzed and published the prescription in London in 1786 The use of Fowler's solution (potassium arsenite solution U S P), as it has since been known, helped to raise arsenic compounds again to a status of medicinal respectability One need not discuss at length the importance attained by arsenic compounds with the introduction of arsphenamine ("salvarsan") by Ehrlich for the treatment of syphilis This importance was enhanced by the later development of neoarsphenamine (neosalvarsan®) and the more recent oxophenarsine hydrochloride (mapharsen®) At one time or another arsenic compounds were employed in the treatment of nearly all dermatoses They undoubtedly have some beneficial effect in many diseases Their general use was soon limited, however, by the recognition of their occasional harmful effects, such as keratoses, epitheliomas, arsenical dermatitis and visceral complications In the treatment of syphilis, however, arsenic compounds long remained unchallenged With the advent of penicillin, it seems at present as if arsenical drugs will be replaced completely even in the treatment of that disease Only time will tell whether treatment with penicillin, effective as it is in quickly rendering a syphilitic patient noninfective, will need to be followed by chemotherapy in order for one to obtain the highest possible percentage of long range cures or remissions

Arsenic compounds are still being used frequently in diseases other than syphilis Neoarsphenamine and oxophenarsine hydrochloride are

group of patients to investigate fully the effects of a drug, with the controls essential to an accurate appraisal Many clinical investigators as yet lack the mature judgment needed to temper their enthusiasms and to keep them from being carried away by clinical impressions that may not be lasting In dermatologic therapy too many are attempting to run who have not yet fully mastered the art of walking It may seem antiquated to use old drugs and old fashioned to treat patients with the simple purpose of getting them well as quickly as possible Certainly there is more glamour in being up to the minute with the use of the newest drugs and even ahead of the times in the investigation of drugs for which no specific use has yet been found Most of us dermatologists, in my opinion, are most useful, however, when we devote ourselves wholeheartedly to the career of being healers of the sick It is an old-fashioned role, devoted largely to treating diseases that are not new and most often calling for the employment of drugs that have been tested in the crucible of time It is an honorable career and a satisfying one, a career to which, in our highly scientific age, we particularly need converts.

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used in the treatment of sarcoid, tuberculosis indurativa, papulonecrotic tuberculid and lupus erythematosus, often producing considerable improvement Injections of solutions of ferric cacodylate or sodium arsenate have been employed in the treatment of pemphigus Acetarsone tablets taken by mouth have at times been effective in the treatment of pemphigus and lichen planus Asiatic pills (composed of arsenic trioxide and black pepper) and potassium arsenite solution, however, have been the most popular forms of administering arsenic by mouth, and they have been used especially in the treatment of lichen planus, dermatitis herpetiformis, neurodermatitis, urticaria papulosa, pompholyx, parapsoriasis and vitiligo In the treatment of psoriasis the use of arsenical drugs should be discouraged, for they need to be administered for too long a time to be devoid of danger It must be remembered, however, that in some persons the use of arsenic compounds for even a short period may be followed by serious sequelae

Iodine in the form of a solution of potassium iodide given by mouth is still an important adjuvant treatment of late syphilis It has also been recommended as an adjuvant to streptomycin in the treatment of tuberculosis It is an excellent remedy in cases of blastomycosis, sporotrichosis, actinomycosis, kerion celsi and other deep fungous infections At times it is effective in the treatment of arthropathic psoriasis or resistant psoriasis, a use which is seldom remembered at present In the form of strong iodine solution U S P or iodoform pills it is helpful at times in treatment of cases of lupus erythematosus Intravenous injections of a solution of sodium iodide often relieve the pain of herpes zoster

Mercurial preparations are seldom used at present in the treatment of syphilis As a therapeutic test in late syphilis, however, the oral administration of mercury and chalk tablets is very useful The oral administration of mercury with chalk or yellow mercurous iodide is often effective in the treatment of juvenile warts and lichen planus, while mild mercurous chloride is an excellent cathartic in the treatment of urticaria and toxic erythema

Bismuth compounds given by intramuscular injection have long been used in the treatment of syphilis While at present displaced by penicillin, they are still being employed in the supplementary chemotherapy of that disease In lupus erythematosus and lichen planus they are often effective, either alone or combined with arsenic as in bismuth arsphenamine sulfonate (bismarsen®)

Gold, in the form of intravenous injections of gold and sodium thiosulfate or other gold compounds, is still probably the most effective drug in the treatment of chronic discoid lupus erythematosus, although the percentage of failures with its use is increasing as the years go by

SPECIFIC SENSITIVITY TO FOODS AS A FACTOR IN VARIOUS TYPES OF ECZEMATOUS DERMATITIS

CLARENCE S LIVINGOOD, M D
GALVESTON, TEXAS
AND
DONALD M PILLSBURY, M D
PHILADELPHIA

MANY observers[1] have reported cases of chronic, recurrent, vesicular eruptions of the hands due to various food allergens Other authors,[2] who have written on the problem of eczematous dermatitis of the hands, designated by various terms such as "chronic eczematoid dermatitis of the hands" and "recurrent vesicular eruptions of the hands," have listed food allergy as one of the infrequent and relatively unimportant etiologic factors Stokes,[3] in particular, emphasized the concept that such eruptions of the hands, as well as chronic eczematous dermatitis at other sites, are often due to multiple etiologic factors He stressed the importance of a "factorial analysis" in the study of such patients and included food allergy among the various etiologic considerations

Read at the Sixty-Eighth Annual Meeting of the American Dermatological Association, Inc, San Diego, Calif, April 27, 1948

From the Department of Dermatology and Syphilology, Graduate School of Medicine, University of Pennsylvania, Dr Donald M Pillsbury, Director

For many of these patients, scratch, intradermal and patch tests were done by Dr Norman R Ingraham Jr Our associate, Dr Malcolm C Spencer, assisted in the management of some of the patients included in this series

1 Buckley, L D Diet and Hygiene in Diseases of the Skin, J A M A **59** 535 (Aug 17) 1912 Wise, F, and Wolf, J Dermatophytosis and Dermatophytids, with Particular Reference to Differential Diagnosis of Dyshidrosiform Eruptions of Hands and Feet, Arch Dermat & Syph **34** 1 (July) 1936 Wise, F, in discussion on Lehmann, C F Acute Vesicular Eruptions of the Hands and Feet, ibid **21** 499 (March) 1930 Engman, M F, Jr, in discussion on Andrews, G C, Berkman, F W, and Kelly, R J Recalcitrant Pustular Eruptions of Palms and Soles, ibid **29** 548 (April) 1934

2 Lane, C G, Rockwood, E M, Sawyer, C S, and Blank, I H Dermatoses of the Hands, J A M A **128** 987 (Aug 4) 1945 Callaway, J L, and Barefoot, S W The Diagnosis and Management of Chronic Eczematoid Dermatitis of the Hands, North Carolina M J **1** 547, 1940

3 Stokes, J L, Lee, W E, and Johnson, H M Contact, Contact-Infective and Infective Allergic Dermatitis of the Hands, with Especial Reference to Rubber Glove Dermatitis, J A M A **123** 195 (Sept 25) 1943

Antimony, as antimony potassium tartrate or stibophen (fuadin®), seems to be outdated in the treatment of granuloma inguinale as a result of the introduction of streptomycin Antimony potassium tartrate is still being used, however, in treatment of cases of mycosis fungoides and pemphigus foliaceus

Intravenous injections of a 10 per cent solution of sodium thiosulfate are sometimes of benefit in the treatment of disseminated neurodermatitis In the treatment of arsenical exfoliative dermatitis, however, that drug has largely been displaced by BAL (2,3-dimercaptopropanol)

Sodium salicylate given by mouth is often effective in treatment of cases of erythema multiforme and erythema nodosum, while phenyl salicylate is more often recommended for urticaria, and salicin for psoriasis Acetylsalicylic acid, alone or in combination with codeine, forms one of the most effective drugs for the relief of pain in herpes zoster

In the treatment of urticaria and other allergic dermatoses the antihistaminic drugs seem to have successfully eliminated all drugs used formerly In the urticaria that results from penicillin, however, epinephrine is often necessary for quick relief and at times ephedrine is also helpful In individual cases benefit may also be obtained after the employment of bile extracts, belladonna tincture, cascara sagrada, magnesia magma, mild mercurous chloride, phenobarbital or calcium gluconate injection

Quinine has been used in the treatment of severe acne vulgaris and resistant cases of lupus erythematosus

Foreign protein therapy, in the form of administration of bactalbumin (aolan®), a solution of peptones and proteoses derived from milk (proteolac®), milk, intravenous injections of typhoid vaccine or autohemotherapy, is often of great value for severe acne vulgaris, neurodermatitis, dermatitis venenata, psoriasis and dermatitis herpetiformis, although for the last-mentioned disorder sulfapyridine has proved to be the most effective drug in cases in which it can be employed

Of the sedatives, phenobarbital is probably the most widely prescribed drug, but at times bromides, chloral hydrate or paraldehyde are more effective when prolonged sedation is desired

Sodium chloride is indicated in the treatment of bromoderma and bromine acne It is effective in the enteric-coated tablets, and it seldom needs to be given intravenously

Vaccine therapy still has its supporters in treatment of recurrent furunculosis and pyodermas, and its employment is not completely outdated by the introduction of penicillin and the sulfonamide compounds Smallpox vaccine is often beneficial in cases of recurrent herpes zoster

In 1946, Rowe [4] reported a series of 80 patients (42 per cent of 182 patients with eruptions of the hands) with "atopic dermatitis of the hands" due to food allergy, and concluded from his observations that "dermatitis of the hands in the average population may result more frequently from atopic allergy to food than from any other cause"

At about the same time, Flood and Perry [5] reported two series of patients, 30 patients with "recurrent, vesicular eruptions of the hands" being discussed in one paper,[5a] and 13 patients with "eczematoid dermatitis" in the other,[5b] with food sensitivity comprising the primary etiologic factor Flood and Perry did not attempt to estimate the exact incidence of food allergy as the predominant factor in such eruptions, nor did they compare its importance with other factors, but they implied that specific sensitivity to foods is at least as important as any other etiologic factor

Our experience in the study and treatment of eczematous dermatitis of the hands, feet and other sites is recorded in this paper with an attempt at a critical evaluation of the relative importance of specific food sensitivity as a primary or contributory etiologic factor in such eruptions One of us (C S L) had an opportunity to accumulate considerable experience in this therapeutic approach during World War II, but none of the patients encountered at that time is included in this report because adequate follow-up was not possible All the patients in this series were seen and followed in our joint private practice We have included only those patients with an adequate period of follow-up observation and in whom a predominant role of food allergy in the eruption seemed inescapable Furthermore, we have not included patients from whom complete cooperation was not obtained This fact has limited the number of patients in our series, but it is believed that the experience with this group is representative and the major aspects of this subject are illustrated in the case material It is believed that one reason for some difference of opinion in regard to the importance of the food allergy factor in eczematous dermatitis is the failure to realize that food sensitivity is only one of the etiologic agents in many of these cases and that the complete cure and, indeed, recognition of a contributory food allergy factor depend on the identification and adequate management of all the factors concerned in the individual case This principle is well illustrated in many of our cases

It is essential to attempt to clarify the descriptive terms applied to this group of eczematous eruptions because nomenclature is cumbersome

4 Rowe, A H Atopic Dermatitis of the Hands Due to Food Allergy, Arch Dermat & Syph **54** 683 (Dec) 1946

5 (*a*) Flood, J M , and Perry, D J Recurrent Vesicular Eruptions of the Hands Due to Food Allergy, J Invest Dermat **7**·309, 1946, (*b*) The Role of Food Allergy in Eczematoid Dermatitis, Arch Dermat & Syph **55**.493 (April) 1947

Of the endocrine substances thyroid is probably used most often It is especially indicated in the treatment of myxedema and hypothyroid loss of hair, but it is also prescribed for scleroderma, onychodystrophy and, at times, for acne Posterior pituitary injection (pituitrin®), 0 25 cc (obstetric dose) given subcutaneously daily, often relieves the pain in herpes zoster and hastens the involution of the disease

Dilute hydrochloric acid is prescribed in cases of rosacea accompanied with achlorhydria

Iron compounds given by mouth, hematinic tablets and injections of crude liver are often valuable in the treatment of severe acne vulgaris, lupus erythematosus and pemphigus, but in the last-mentioned disease a blood transfusion is probably the most rapid procedure for improving the hematologic status of the patient

Preparations of the vitamin B complex, dried yeast and extract of rice polishings are used in the treatment of glossitis, perlèche, pellagra and rosacea, while vitamin A preparations are often beneficial in treatment of cases of keratosis follicularis, keratosis pilaris, ichthyosis and pityriasis rubra pilaris

DRUGS FOR TOPICAL USE

It is in topical therapy that we dermatologists have our greatest heritage It is in this field also that great skill in therapy can be acquired most rapidly by the intelligent interpretation of experience The surface location of cutaneous lesions, the ease of applying many forms of medication and the ready observation of the effects of local applications make the skin an ideal experimental organ A novice who studies minutely the clinical features of all cutaneous lesions and remembers well how they react to different drugs in various concentrations and in diverse vehicles soon has acquired the therapeutic wisdom of a veteran The careful selection of a few effective drugs and their adaptation to the treatment of various diseases in all stages of activity is much more educational than an aimless but wishful flitting from one proprietary mixture to a later one

In cases of generalized pruritus baths may be used to make a patient more comfortable. Cool colloid baths, prepared with starch, bran or oatmeal, are soothing to an inflamed skin Tar baths are antipruritic and at times are also helpful in treatment of extensive psoriasis Baths containing potassium permanganate are useful in the therapy of widespread pyodermas and of pemphigus

Cold wet dressings are often the most soothing form of treatment in acute inflammations of the skin Skim milk containing boric acid is nearly always well tolerated A saturated aqueous solution of boric acid is effective and inexpensive, while aluminum acetate solution

and confusing, especially for the physician who is not a dermatologist The same type of disease process has been referred to by various authors as eczema (with numerous qualifying terms such as vesicular and nummular), eczematoid dermatitis of the hands and feet, chronic, vesicular eruptions of the hands, "atopic dermatitis of the hands" and "eczematous contact-type allergic dermatitis," among other terms It would be desirable to use terms based entirely on etiology, but this is not possible because the cause in many cases is unknown, in other instances the etiologic agents are multiple, and they may vary from time to time in the same patient Therefore, any classification must be partly etiologic and partly morphologic There is general agreement in the use of the following terms (or various synonyms), either because the dermatitis is due to a single etiologic factor or because of the characteristic type, distribution and course of the cutaneous eruption (1) contact dermatitis, (2) dermatitis medicamentosa (eruptions due to drugs), (3) atopic dermatitis, (4) infantile eczema of atopic type, (5) seborrheic dermatitis and (6) lichen simplex chronicus

We use the term eczematous dermatitis as a morphologic diagnostic term for all other types of chronic and recurrent dermatitis due to a wide variety of external and internal causes or of unknown etiology It is the group of cases in this category which has been responsible for most of the confusing synonyms The individual entities within the syndrome are often not sharply defined, and transitional types are encountered For example, it may be difficult to determine whether the patient has a contact dermatitis with secondary bacterial infection, or a pyoderma with secondary eczematous changes due to sensitization to bacteria, or reactions to local treatment

The cataloging of the individual patient into a distinct diagnostic category depends on qualification of the term by adding the site or sites of involvement and the etiologic factors, if they are determined and proved (so far as doing so is possible) The following etiologic factors are variously recognizable in (chronic) eczematous dermatitis

1 Allergic contactant
2 Primary irritant
} (Dermatitis in which these factors are the only factors is classified under the heading of contact dermatitis)

3 Food allergy

4 Secondary bacterial invasion and sensitization (Impetigo and other primary uncomplicated pyogenic infections of the skin are not included)

5 Drug allergy (If this is the only factor the condition should be included under the heading of dermatitis medicamentosa)

6 Pollen and inhalant allergy

7 Mycotic infection and mycotic sensitization (Uncomplicated primary fungous infection and dermatophytids are classified as such)

8 Psychosomatic, traumatic, thermal, endocrine, peripheral, vascular and dyshydrotic factors and foci of infection

9 Undetermined etiologic factors

(in a dilution of 1 to 16) and a combination of the two are extremely popular In treatment of dermatitis due to plants, solutions of lead acetate (1 teaspoon to 1 quart), potassium permanganate (1 to 5,000) or strong tea generally bring relief In treatment of pyoderma or acute tineal infection of the feet alibour water (water containing zinc and copper sulfate, 1 to 20) or potassium permanganate (1 to 5,000) are of great value Solutions of silver nitrate (1 to 500 or 1 to 1,000) are efficacious in the therapy of acute oozing dermatitis and the weeping streptococcic dermatitis seen on the legs or behind the ears

Of the drying lotions, calamine lotion and starch lotion, with or without the addition of phenol and menthol, are the most widely used When the skin is to be kept from becoming too dry, calamine liniment or lime liniment may be used

Most powders contain starch, boric acid and talc, at times with the addition of other medicaments for specific purposes, such as salicylic acid and thymol in treatment of tineal infections

Soothing ointments include petrolatum, rose water ointment, hydrous wool fat, theobroma oil, lead oleate ointment, zinc oxide ointment and zinc oxide paste

Effective antiperspirants are a 25 per cent solution of aluminum chloride, a 1 per cent solution of formaldehyde and, for the feet, a 1 4,000 solution of potassium permanganate

Mercury is still one of the most efficacious drugs for topical use on the skin Except for the few persons who are sensitive to the drug, ammoniated mercury in the form of a 3 per cent to 10 per cent ointment is probably the most suitable medication for impetigo, ecthyma and other pustular infections of the skin Five per cent ammoniated mercury ointment is often rapidly effective in treatment of infected eczema of the auditory canal, and it is also well tolerated in treatment of impetiginized atopic dermatitis Its use is often beneficial in cases of psoriasis and seborrheic dermatitis One per cent ointment of yellow mercuric oxide is useful in treatment of seborrheic dermatitis of the eyelids, and in therapy of pediculosis of the eyelids it is unexcelled A 1 to 5,000 aqueous solution of mercuric oxycyanide is also an effective and clean treatment for seborrheic dermatitis of the eyelids A 1 to 1,000 solution of mercury bichloride has much support for its use in the treatment of folliculitis and also as an ingredient of scalp lotions

In the treatment of sycosis vulgaris an occasionally more effective antiseptic is quinolor® (chlorohydroxyquinoline) At times, however, its employment is followed by a dermatitis Drugs that are also excellent in the treatment of folliculitis, impetigo, ecthyma and other pyodermas are 1 per cent to 3 per cent ointment of iodochlorohydroxyquinoline (vioform®) and 3 per cent to 10 per cent ointment of bismuth tribromo-

It is realized that there are other possible contributory factors, such as physical allergies, diseases of the gastrointestinal tract, liver or kidney, intercurrent infections of various types and metabolic disturbances

METHOD OF STUDY

It is our practice to consider specific food sensitivity as a possible primary or contributory factor in all cases of eczematous dermatitis, regardless of the site of involvement, unless it is obvious on initial examination or a brief subsequent period of observation that other causes are responsible

The methods of study in regard to a possible food allergy factor which we have used include one or more of the following regimens

(1) A strict trial diet (as outlined by Flood and Perry,[5]) which is feasible only for hospitalized patients

(2) A so-called basic "nonallergenic diet," consisting of beef, lamb, chicken, canned pears, canned apricots, prunes, baked or boiled potatoes, lettuce, celery, string beans, red beets, lima beans, weak tea, sugar, salt, white vinegar, ry-krisp® or pure rye bread, peach preserves and apple jelly, followed by addition of foods one at a time at five-day intervals after a base line of improvement has been established

(Recently, following the suggestions of Winston and Sutton,[6] we have added only one food at each meal [For example, on the first day of the diet, the menu is as follows Breakfast canned pears, luncheon—canned pears and tea with sugar, and dinner canned pears, tea with sugar and lamb On subsequent days other foods of the basic diet are added in a similar manner] If pruritus and/or new lesions of any type are noted after the addition of a new food, all new foods which have been added in the previous twelve-hour period are eliminated from the diet)

(3) A minimal elimination diet ("spot" elimination diet), interdicting sea foods, chocolate, nuts, citrus fruits, tomatoes, pork, cheese and coffee

(4) A diet diary

It must be realized that considerable individualization is necessary, inasmuch as there are practical limitations in the study and treatment of patients from the standpoint of food allergy A high percentage of patients do not like strict diets, hospitalization is not available or feasible for everyone, and, on an outpatient basis, business and social responsibilities make it difficult for persons to follow even simple elimination diets There are very few patients who find it possible to eat all their meals at home, and, if they do, the necessity of special cooking for one member of the family is a complicating factor Furthermore, the vast majority of patients are not easily convinced that food allergy may constitute a factor in their particular case Only a small number of our patients will follow diets as limited as the Rowe elimination diet[6] or the so-called "basic nonallergenic" diet for more than two

6 Winston, B H, and Sutton, R L, Jr Dermatitis of the Hands Due to Ingested Allergens, Arch Dermat & Syph **58** 335 (Sept) 1948

phenate (xeroform®) Dermatitis from the latter two is uncommon, and their employment generally brings gratifying results With rare exceptions it should not be necessary for one to use preparations of the sulfonamide drugs or penicillin topically in the treatment of cutaneous infections These preparations are seldom as effective topically as the drugs previously mentioned, and their use in this form is hazardous

Sulfur has an old and honored place in dermatologic therapy For seborrheic dermatitis it still is the most effective medication, either alone in a 3 per cent to 5 per cent ointment or with the addition of 1 per cent to 3 per cent salicylic acid In various sulfur lotions, such as white lotion, sulfurated lime solution or Kummerfeld lotion (a compound containing camphor spirit, alcohol, tragacanth, precipitated sulfur and distilled water), it has retained its popularity in the treatment of acne Scabies may still be cured by the application of sulfur in a 3 to 10 per cent ointment A 15 per cent solution of sodium thiosulfate will cure tinea versicolor without any messing The pruritus of dermatitis herpetiformis is often relieved by application of a 2 per cent sulfur ointment In the form of a 30 or 40 per cent sulfur paste, sulfur is frequently beneficial in the therapy of seborrheic dermatitis, dermatitis herpetiformis, chronic eczema and other chronic dermatoses

Tar is a remedy of great value for many dermatoses In nummular eczema and infantile eczema coal tar ointment generally produces rapid improvement, and in eczema of the nipple the response is excellent Tar ointments are beneficial in treatment of tineal infection of the hands and feet and at times also in that of psoriasis and recalcitrant eruption Solutions of crude coal tar in acetone, chloroform or collodion are much cleaner to apply but are not as effective as the ointment form The various distilled or decolorized tars are also much less effective than crude coal tar, but distarol® and zetar® are comparatively good clean substitutes The wood tars (pine tar, juniper tar and rectified oil of birch tar) should be used only in chronic dermatoses, for their employment in more acute stages generally increases the inflammation "Oil of cadeberry"[1] has all the benefits of juniper tar, but it has a much more pleasant odor In treatment of resistant patches of psoriasis or lichen chronicus simplex, tar-containing ointments, such as compound ointment of sulfur or Dreuw's ointment (a preparation containing salicylic acid, chrysarobin, rectified oil of birch tar, medicinal soft soap and petrolatum) may be used Tar should never be used in any form in the presence of furuncles or other pustular infections, for fear of the production of lymphangitis Folliculitis from the use of tar can generally be prevented by removal with a bland oil of all the old residue on the skin before a new application is made

1 A product of Muth Bros & Co, Baltimore, containing barbados tar and oil of juniper berry

weeks, and, if there is no significant improvement at the end of that time, there is difficulty in persuading the patient to continue any type of dietary restriction

The evaluation of the course of the eruption is complicated by the fact that the interval between the ingestion of food and the beginning of the exacerbation varies in different patients Furthermore, there is an important quantitative factor, and, in addition, the presence of concomitant pyogenic and pyogenic sensitization, allergic contactant or other factors interferes with the interpretation of results

It was shown by many investigators [7] that limitation of the diet on the basis of scratch tests to food is rarely helpful, and our experience is in agreement with this conclusion However, many patients who do not like dietary restrictions in principle will cheerfully adhere to a restricted diet based on the results of scratch tests, often for years

Because of all these limitations, we have been obliged to use various methods of approach, including the strict trial diet as outlined by Flood and Perry, a basic nonallergenic diet which follows the general principles of the Rowe elimination diets and a "spot" elimination diet from which foods with a high allergenic index are eliminated All the patients who were studied by means of the strict trial diet were hospitalized After hospitalization, during which pronounced improvement or complete cure was affected in all patients in whom food allergy was an important etiologic factor, new foods were added at five day intervals Diet diaries were used in all cases because, for one thing, they assist patients in learning to recognize their exacerbations and to correlate them with the addition of possible causative foods

PRESENTATION OF CASES

We have been able to demonstrate either a primary etiologic or an important contributory etiologic food factor in a total of 26 patients who have had adequate follow-up observation For an additional 41 patients, specific sensitivity to food was an apparent important component of the dermatitis, but we were not able to establish unequivocal proof of this fact, or the observation period was not sufficient at the time of writing, and, therefore, their cases are not included in the series which constitutes the basis for our discussion

Lack of space makes it impossible for us to include the individual case histories of all these 26 patients Therefore, only 3 representative cases are presented in detail, pertinent data on all the 26 patients are summarized in the accompanying table

7 (*a*) Winston and Sutton [6] (*b*) Rowe, A H Elimination Diet and the Patient's Allergies A Handbook of Allergy, ed 2, Philadelphia, Lea & Febiger, 1944

Naphthalan and ichthammol (ichthyol®) in 5 to 10 per cent ointments are often helpful in the treatment of many chronic dermatoses

Chrysarobin in a 2 to 10 per cent ointment is useful in the treating of chronic patches of psoriasis and lichen chronicus simplex, while a 4 per cent suspension in chloroform works well in the treatment of chronic paronychia and tineal infections between the toes The drug is sometimes extremely irritating, and it is generally being replaced by anthralin ointment (1/10 to 1 per cent) Other drugs with similar action are pyrogallol, acetpyrogall (triacetyl pyrogallol, lenigallol®), anthrarobin and cignolin

Resorcinol is widely used in combination with sulfur lotions in treatment of acne and also in treatment of seborrheic dermatitis For use on the scalp it is available as resorcinol monoacetate (euresol®)

Salicylic acid is added to many ointments for its keratolytic effect It is an active fungicide, and in benzoic and salicylic acid ointment it probably is still the most effective medication for ringworm infections Thymol may be added (0 25 per cent) to increase the fungicidal activity Fifty per cent salicylic acid in petrolatum has been recommended in the treatment of kerion, but in my experience milder ointments have been as effective Forty per cent salicylic acid plaster is effective in the removal of calluses and corns

Silver compounds are drugs that deserve wider use than they enjoy at present Wet dressings of silver nitrate solution (in a dilution of 1 to 1,000 or 1 to 500) often produce a spectacular drying of acute, weeping streptococcic infections on the legs and behind the ears Ten to 20 per cent solutions are useful for cauterizing fissures, and I have found daily applications of 10 per cent silver nitrate solution extremely helpful in treating ingrown toe nails The granulation tissue is destroyed in these cases and is replaced by a tough crust that resists the pressure of the toe nail In treatment of seborrheic dermatitis of the eyelids a 5 per cent solution of argyrol® (a combination of silver with a protein produced by the electrolysis of serum albumin) dropped into the eye is often helpful Chronic ulcers are effectively treated by the Mikulicz ointment, which contains 1 per cent silver nitrate and 10 per cent Peruvian balsam in petrolatum

Iodine in the form of a 10 per cent ointment in lard in my experience is more efficacious in treatment of ringworm of the scalp than are the newer fatty acids Another old remedy for this disease is a 3 per cent solution of salicylic acid in tincture of iodine In alopecia areata 3 per cent iodine in petroleum benzine has the advantage of staining the skin less than does tincture of iodine or Cutler's fluid (equal parts of liquified phenol tincture of iodine and chloral hydrate) In this disease local applications of phenol, soon removed with alcohol, also act as an adequate irritant

REPORT OF CASES

CASE 1.—M. C., a housewife aged 32, was seen because of a patchy, eczematous dermatitis of twenty years' duration, involving the hands and the left lower eyelid, the eyelid having become involved only within the past four months. The eruption was characterized by erythematous, scaling, oozing, rather well demarcated, vesicular plaques on the right palm and on all surfaces of the right third finger, as well as on the sides and dorsal surface of the second and fifth fingers of the left hand. The patient had severe pruritus, which had interfered with sleep and other activities. Several weeks after she came under our observation, she also had a brief episode of an oozing, pruritic, intertriginous dermatitis of the axilla and groins. At various times vesicopustules and residual pyogenic crusts were noted as a part of the process. This patient had not been completely free of lesions since the onset, although there had been many exacerbations and partial remissions. The longest and most significant partial remission had occurred approximately two years before her first visit, during the time that she was on a reducing diet consisting of grapefruit juice, eggs, toast, cheese, tea, lettuce and tomatoes. On several occasions during the past three years, she had had attacks of intertriginous dermatitis in the axilla and groins persisting for two to three weeks, followed by a complete remission.

The patient had been treated by at least twelve different physicians, including five dermatologists, who had given her a total of approximately twenty-five roentgen ray treatments, and she had been informed by one of her physicians that he had given her as much roentgen therapy as her hands would tolerate. The use of numerous ointments and other types of local treatment, as well as the employment of a soap substitute and strict avoidance of soap and water and all household contactants, had had no apparent effect on the course of her lesions.

There was a history of infantile eczema in early infancy and of relatively transient attacks of acute urticaria in childhood. The familial allergic history was noncontributory except that the patient's sister had had apparent hydrorrhea due to vasomotor neurosis (vasomotor rhinitis) and urticaria.

The management and course of this patient's eczematous dermatitis during the eighteen months of observation were as follows:

1. Patch tests with numerous household contactants, cosmetics and routine test materials had negative results except for 1 plus reactions to dilutions of 1: 1,000 of bichloride of mercury, prell® shampoo, lustre creme® shampoo, rinso® and resorcin, although all these reactions were minimal.

2. Initially, on an outpatient basis, the patient was placed on a diet of baked potato, beef, lamb, string beans, carrots, tea, sugar, grapefruit juice, boiled eggs, canned pears, prunes, canned apricots, lettuce and tomatoes. In addition, she was asked to avoid prell® shampoo, lustre creme® shampoo, and rinso®. Local treatment consisted of potassium permanganate soaks and 3 per cent ichthammol (ichthyol®) in zinc oxide ointment. Housework of all types was reduced to a minimum by the patient's employing a full time maid and enlisting the cooperation of her husband for dishwashing when the maid was not available. She did not have significant, sustained improvement on this regimen of treatment.

3. Therefore, she was hospitalized for a period of two weeks. She was placed on a strict trial diet (Flood and Perry), with sugar water during the first twenty-four hours, baked potato during the next twenty-four hours and lamb during the next twenty-four hours, during this time there was pronounced continued improvement, with almost complete disappearance of pruritus after the first forty-eight hours. Tea was added on the fourth day, and eight hours after the first cup of tea,

Copper in the form of a 10 per cent ointment of copper oleate is therapeutically active in ringworm of the scalp, and alibour water (1 to 20) is an excellent wet dressing for Bockhardt's impetigo and other infected lesions

It is possible that hexachlorocyclohexane in a vanishing cream base (kwell® ointment) will replace all other antiparasitic drugs Until its place has been firmly established and its possible dangers are fully understood, it is well to remember that other good remedies for scabies include sulfur, Peruvian balsam and its derivative, benzyl benzoate, betanaphthol, and storax

Benzoin tincture is often applied to fissures A 50 per cent ointment of benzoin tincture is an excellent remedy for chronic ulcers, as is the application of Aloe vera leaf or ointment Urea solution is useful in removing necrotic tissue from ulcers Cod liver oil ointments are efficacious in the treatment of chronic ulcers and of burns, and for burns trinitrophenol solution is rapidly effective in treatment of patients who can tolerate it

Of the various dyes used for topical application, Castellani's paint (a preparation containing basic fuchsin, phenol, boric acid, acetone and resorcinol) is by far the most valuable in the treatment of tineal infections on moist areas It is best to begin by using a 25 per cent strength paint and then to strengthen it gradually A 1 per cent solution of methylrosaniline chloride is excellent in treatment of yeast infections, especially those on the webs of the fingers and in the folds of the skin and paronychia A 5 per cent solution of methylrosaniline chloride in 20 per cent alcohol is effective in the prevention of infection at the site of removal of warts or moles Five per cent scarlet red ointment is an old and effective remedy for chronic ulcers

For screening agents in lupus erythematosus and sensitivity to light, preparations of phenyl salicylate, quinine or tannic acid are satisfactory and are less likely to produce dermatitis than sodium para-aminobenzoate (Paba®) cream

The application of 10 per cent bergamot oil in alcohol followed by exposure to the ultraviolet rays at times hastens the return of pigment in patches of vitiligo

Five per cent ethyl aminobenzoate (benzocaine®) in flexible collodion applied to insect bites relieves the pruritus in many cases

Condyloma acuminatum is best treated by the application of 25 per cent podophyllum resin in alcohol One must exercise great care not to treat too large an area at one time, for fear of producing severe inflammation

Verrucae under the nails or about the nails may be treated by applying 4 per cent formaldehyde solution, sulfurated lime solution or mono-

Data Concerning Twenty-Six Patients with Eczematous Dermatitis

Case No	Age	Sex	Occupation	Duration	Period of Observation	Sites of Involvement	Methods of Study	Factors	Foods Which Caused Exacerbation	Comment
1	32	F	Housewife	20 yr	18 mo	Hands, left lower eyelid, axillas, groins	Hospitalization, strict trial diet, diet diary	1 Food allergy 2 Pyogenic infection and pyogenic sensitization	Tea, apricots, broccoli, cauliflower, cabbage, peaches	Pyogenic factor treated with penicillin administered parenterally
2	29	F	Nurse and housewife	1 yr	6 mo	Hands, left lower eyelid	Basic "nonallergenic" diet, diet diary	1 Food allergy 2 Contactant	Eggs, milk	Onset as contact dermatitis
3	30	F	Secretary	15 mo	1 yr	Feet, hands	Basic "nonallergenic" diet, diet diary	1 Food allergy	Wheat, chocolate, coffee, shrimp, crab, lobster	Scratch test-negative diet partially successful
4	28	M	Mail carrier	4½ yr	9 mo	Hands	Hospitalization, strict trial diet, diet diary	1 Food allergy 2 Pyogenic infection and pyogenic sensitization	Milk, chocolate, pork, tomatoes	Pyogenic factor treated with parenterally administered penicillin combined with fever therapy
5	44	M	School teacher	1 yr	3 mo	Perianal region, scrotum, hands	Spot elimination diet, diet diary	1 Food allergy	Chocolate, shad, shrimp	No resemblance of scrotal dermatitis to lichen simplex chronicus
6	30	F	Secretary and housewife	6 mo	4 mo	Hands	Basic "nonallergenic" diet, diet diary	1 Food allergy	Cinnamon, onions, eggs, smoked ham	
7	55	F	Housewife	6 mo	2 yr	Hands	Spot elimination diet, diet diary	1 Food allergy 2 Contactant	Nuts, grapefruit, oranges	Prominent psychogenic factor
8	27	M	Medical student	2 mo	16 mo	Hands	Hospitalization, strict trial diet, diet diary	1 Food allergy 2 Contactant 3 Drug	Wheat, milk, pork(?), chicken(?), carrots(?)	Exacerbations with use of naphazoline ("privine") nose drops, patient not cured until smoking was discontinued, positive reaction to patch test with tobacco
9	67	M	Civil engineer	1 yr	17 mo	Legs, ankles, thighs, hands, left upper and lower eyelids	Basic "nonallergenic" diet, diet diary	1 Food allergy	Wheat, veal, rye	No improvement until responsible foods were discontinued for several weeks—which observation is unusual
10	37	F	Housewife	6 yr	20 mo	Hands	Hospitalization, strict trial diet, diet diary	1 Food allergy 2 Pyogenic infection and pyogenic sensitization 3 Drug	Broccoli, string beans, lima beans, vanilla, peas, sweet corn	Exacerbation on ingestion of sulfadiazine and pentobarbital sodium, acetylsalicylic acid, pyogenic factor treated with penicillin given parenterally
11	31	F	Housewife	4 mo	9 mo	Hands, legs	Basic "nonallergenic" diet, diet diary	1 Food allergy	Wheat, chocolate peaches(?), pork(?)	Unusually severe, extensive involvement, with rapid improvement on management on an outpatient basis
12	30	F	Secretary	5 mo	18 mo	Hands	Spot elimination diet, diet diary	1 Food allergy	Grapefruit, peanuts, oranges	Prominent psychogenic factor
13	4	M	Preschool child	1 yr	6 mo	Buttocks, legs	Basic "nonallergenic" diet, diet diary	1 Food allergy	Eggs, chocolate, pork	Exacerbations on numerous attempts to add causative foods to diet
14	50	M	Executive	1 yr	1 yr	Hands, legs	Hospitalization, strict trial diet, diet diary	1 Food allergy	Almonds, tomatoes, pork, Scotch whisky, oranges(?)	Patient completely incapacitated by his dermatitis

chloroacetic acid Applications of trichloroacetic acid remove patches of xanthelasma Monochloroacetic acid may be used in destroying seborrheic verrucae After the Sherwell removal of an epithelioma solution of mercuric nitrate or ferric subsulfate solution may be applied

For Vincent's infection of the mouth the administration of penicillin troches is no doubt the most effective local treatment It is a mistake, nevertheless, for one to form the habit of using penicillin routinely in all oral conditions In most of them nothing is accomplished by penicillin that cannot be performed as well and more safely by mild mouth washes, such as sodium bicarbonate, magnesia magma or the N F antiseptic solution As a local astringent a mixture of kino tincture and myrrh tincture has a well founded reputation

Finally, for the treatment of itchy legs nothing brings relief as rapidly as the application of Unna's paste boot

Many additional drugs have been recommended for the treatment of various dermatoses I have excluded them from this listing either because I did not have personal experience with their use or because they duplicated without advantage other drugs that are more readily available in the average pharmacy

COMMENT

I feel certain that the medications listed have found great success in the work of some dermatologists and have been complete failures with others The fault is not entirely with the drug, for each drug is but an inanimate servant, capable only of performing the limited tasks within its scope The selection of the particular drug and the determination of the proper concentration, the ideal vehicle and the best method of application are often the factors that decide the therapeutic results In addition, the unmeasured ingredient of every medication is the attitude of the physician who prescribes it Some dermatologists have the power to inspire confidence and to obtain from the patient full cooperation in the carrying out of carefully outlined instructions For one to tell a patient merely to put on cold wet dressings, for example, is to assume that the descriptive command means to him the same as it does to the physician A patient is more likely to perform his duties correctly if he is permitted to explain to the physician just how he plans to carry out the orders and is then corrected Only by making certain that the patient is going to use the medications as prescribed can one hope to obtain the anticipated results This added point may seem trivial to some, but one may also expect much better results from medication prescribed with an air of confidence than from that given with a skeptical attitude that almost dares the patient to get well

I should not like to be set down as an obstinate reactionary, intolerant of all that is new Certainly the sulfonamide compounds, antibiotics,

15	56	F	Secretary	1 mo	1 yr	Hands, forearms, neck, right upper eyelid	Basic "nonallergenic" diet, diet diary	1 Food allergy	Oranges, grapefruit, wheat, coffee(?), eggs(?), pineapple(?)	Prominent psychogenic factor
16	56	F	Secretary	10 yr	6 mo	Right upper eyelid, right postauricular area	Spot elimination diet, diet diary	1 Food allergy	Chocolate, lobster, clams, crab	Exacerbations following ingestion of food, accompanied with nausea and gastrointestinal pain
17	22	F	Salesgirl	11 yr	8 mo	Hands	Scratch test-negative diet, diet diary	1 Food allergy	Cheese, pimento, pork pecans	The only patient in our series for whom a scratch test-negative diet was successful, happened to result in the elimination of all causative foods
18	12	M	Student	3 mo	1 yr	Posterior surface of neck	Spot elimination diet, diet diary	1 Food allergy	Chocolate	Repeated exacerbations on addition of chocolate to diet, after six months patient able to eat chocolate occasionally without exacerbation
19	52	M	Executive	6 mo	8 mo	Hands	Basic elimination diet, diet diary	1 Food allergy 2 Pyogenic infection	Rice	Clearing of bacterial infection along with improvement of dermatitis, without specific antibacterial therapy
20	21	F	Secretary	15 mo	6 mo	Hands, right cheek	Basic elimination diet, diet diary	1 Food allergy	Milk, wheat	Repeated sharp exacerbations on addition of milk or wheat products to the diet
21	40	M	Clerk	4 yr	6 mo	Hands	Hospitalization, strict trial diet, diet diary	1 Food allergy 2 Pyogenic infection and pyogenic sensitization	Chocolate, peanut butter	Incomplete clearing until pyogenic factor had been treated with parenterally administered penicillin and fever therapy
22	39	F	Housewife	4 yr	2 yr	Hands, feet	Hospitalization, strict trial diet, diet diary	1 Food allergy 2 Pyogenic infection and pyogenic sensitization 3 Contactant	Pepper, cinnamon, chicken, bacon, smoked ham, onions, paprika	Persistence of sensitivity to causative foods for as long as eighteen months after clearing of eruption
23	28	F	Secretary	3 yr	1 yr	Face	Hospitalization, strict trial diet, diet diary	1 Food allergy 2 Drug	Rice, butter, sweet potatoes, carrots, tomatoes, oranges, eggs, chocolate	Eczematous and folliculopustular lesions, repeated exacerbations after ingestion of vitamin B complex capsules
24	20	F	Nurse	2½ yr	2 yr	Left axilla	Hospitalization, strict trial diet, diet diary	1 Food allergy 2 Contactant	Oranges, grapefruit	Eruption resembling a fixed drug eruption
25	12	M	Physician	3½ yr	6 mo	Hands	Hospitalization, strict trial diet, diet diary	1 Food allergy 2 Contactant 3 Drug	Tomatoes, oranges, grapefruit	Phenobarbital, both as contactant and ingestant, one of the etiologic factors
26	28	M	Foundry worker	3 yr	9 mo	Hands, ankles	Hospitalization, strict trial diet, diet diary	1 Food allergy	Pork, milk, potatoes	Onset of dermatitis, on the dorsal surface of the hands, as a contact dermatitis due to a primary irritant, persistence for years (five) and complete disappearance on elimination of causative foods, repeated exacerbations demonstrated on addition of responsible foods, flare ups within fifteen to thirty minutes after ingestion of causative food

antihistaminic agents and other new drugs have opened new roads to hope in the treatment of many diseases hitherto serious in their prognosis In many instances more progress can be made in hours with the use of new drugs than was possible in months with old-fashioned treatment The risk of sensitization and toxicity inherent in many of these drugs makes it prudent, however, that they be used only when they are needed Not only dermatologists, but also physicians lacking dermatologic training, have tended too much in recent years to try these new drugs as the first medication in the treatment of all dermatoses before turning to older drugs that have proved adequate Furthermore, because of the vital importance of sulfonamide compounds and antibiotics in the treatment of dangerous infectious diseases, it is imperative that these drugs be reserved, if possible, for exigencies when they are desperately needed We dermatologists are seldom called on to treat diseases so serious as to warrant the risk of exhausting a patient's capacity for using a drug that might in the future prove to be life saving

A dissertation on good dermatologic therapy utilizing well established drugs would be incomplete if it failed to stress the most important requisites for obtaining good therapeutic results, namely the correct diagnosis of the disease and the proper appraisal of the stage of activity present One must recognize, for example, not merely that he is dealing with a tineal infection of the feet before instituting proper treatment, it is just as important for one to ascertain whether therapy should be actively fungicidal, in the chronic stage of the disease, or merely soothing, when the skin is acutely inflamed It is important for the physician to recognize the clinical picture of overtreatment dermatitis that may be masking the features of the original dermatosis Discontinuing all previous medication in such cases and the cautious use of soothing treatment will often give the patient great relief and may also bring to light the diagnostic features present One should, in addition, always keep in mind that he is treating a patient with a cutaneous disorder rather than merely treating a cutaneous disease All of us need constant reminding that the skin is often a window to internal disease A dermatologist's diagnostic eye and therapeutic acumen should encompass not only the skin but also the patient living within it

Finally, a clinical dermatologist's chief function (and most of us are primarily clinicians) is to bring to his patients relief from suffering To this end he should utilize all measures of established merit that apply to each case For this vocation most of us are well trained It has become popular in recent years, however, for many dermatologists to become clinical investigators for every new drug and proprietary mixture that is brought to market For this highly critical function most of us are not adequately equipped Not many have a large enough

an interval during which the patient had had 3 cups, there was a sharp, distinct, relatively severe exacerbation, characterized by intense pruritus and recurrence of erythema, vesiculation and oozing Within a brief period evidence of secondary bacterial infection was noted After this episode, 50,000 units of penicillin every three hours was administered for five days, during which time there was a slow but continued improvement At the end of two weeks of hospitalization, the eczematous dermatitis was less active than at any other time since the patient had come under our observation There were no vesicles or pustules, and the pruritus had almost disappeared However, there was some residual scaling, erythema and superficial fissuring The patient was discharged from the hospital, with instructions to follow a diet consisting only of baked potato, lamb and string beans

4 Continued improvement was noted during the next seven weeks except for significant exacerbations following the trial addition of tea and dried apricots to the patient's diet During this time, the diet had been increased to include beef, lamb, string beans, sugar, chicken, turkey, lettuce, asparagus, carrots, baked potatoes, canned pears, prunes, apples, eggs, white bread, saltines, vanilla ice cream, milk and ginger ale All these foods had been added gradually, one at a time, with approximately two to three days between each addition No attempt was made to add further foods during the next month, and during this time the lesions on the hands and eyelids cleared up completely

5 In the next six weeks, in the same manner, the patient added cottage cheese, American cheese, almonds, corned beef, bananas and cherry gelatin, without any exacerbations During this same period she had prompt exacerbations manifested by pruritus, erythema and a few tiny vesicles at previously involved sites, four hours after the addition of broccoli and cauliflower to her diet on two separate occasions

6 During the next six weeks the patient continued to remain free of any signs of involvement except for a slight exacerbation twelve hours after the addition of cabbage and canned peaches to her diet on two separate occasions In the meantime she had added celery, onions, green pepper, mushrooms, beets, mashed turnips, beef and calf liver and several types of fish, so that at this time the only foods restricted from her diet were tea, dried apricots, broccoli, peaches, cauliflower and cabbage

7 During the past year she has been free of involvement and has been able to do all her own housework with no effort to protect her hands from excessive contact with soap and water and other cleansing agents

It is interesting to note that tea has been the main beverage of this patient throughout her adult life because she does not like coffee and, furthermore, that she has always eaten dried apricots

The diagnosis was eczematous dermatitis of the hands, left lower eyelid, axilla and groins, with food allergy (tea, apricots, broccoli, cauliflower, cabbage, and peaches), pyogenic infection and pyogenic sensitization as factors

Comment This is an example of a difficult food allergy problem It is probable that this patient would have been included in the group of those in whom treatment was a failure or, rather, that the food allergy factor would not have been recognizable if it had not been possible for her to be hospitalized and if her cooperation had not been unusually good It may be noted that this patient reacted to several members of the cabbage family, as well as to related fruits She is the only patient in our entire series for whom tea was recognized as a food allergen

A Case for Diagnosis (Mycosis Fungoides? Psoriasis?) Presented by DR JAMES R WEBSTER, DR SAMUEL BLUEFARB and (by invitation) DR N BAKER

Superficial Epithelioma on Sacral Area with Basal Epithelioma near the Anus Presented by DR THEODORE CORNBLEET and (by invitation) DR D COHEN and DR J GRAFFIN

A Case for Diagnosis (Acrodermatitis Chronicus Atrophicans) Presented by DR MICHAEL H EBERT and (by invitation) DR M S KAGEN

Nodular Leukemia Cutis in a 14 Month Old Boy, Duration Eight Months Presented by DR MICHAEL H EBERT and (by invitation) DR N L BAKER

Syringocystoma Presented by DR MICHAEL H EBERT and (by invitation) DR N BAKER

Francis W Lynch, M D, *President*

Leonard F Weber, M D, *Secretary*

June 18, 1947

Adenoma Sebaceum Presented by DR T CORNBLEET and (by invitation) DR H SCHORR and DR J GRAFFIN

R S, a Negro woman aged 23, as a child had frequent episodes of "spasms" which may have been epileptic-like in nature She finished the seventh grade in school at the age of 19 years, and she works as a dishwasher

On May 22, 1947, she entered a medical ward at Cook County Hospital with acute rheumatic fever Subsequently, she had a spontaneous pneumothorax, which is gradually disappearing

Examination reveals an eruption limited to the face which is predominantly on the central portion, chin and eyelids The lesions consist of dark brown papular nodules varying from a few millimeters to 1 cm Neurologic examination revealed no abnormalities Fundoscopic examination has not yet been completed

The Kahn reaction of the blood was negative Urinalysis showed albumin (1 plus) The examination of the blood showed hemoglobin 66 per cent, erythrocytes 3,530,000, leukocytes 5,600, with a normal differential count, and nonprotein nitrogen 22 mg per hundred cubic centimeters The sedimentation rate was 40 mm per hour

The roentgenogram of the chest originally showed a left total pneumothorax, at present there is a 30 per cent residue The roentgenogram of the ankles showed no abnormalities The histologic section from a nodule of the cheek is presented

DISCUSSION

DR M R CARO I agree with the diagnosis both clinically and histologically Histologic examination showed a fibromatous type of tumor rather than hyperplasia of sebaceous glands

DR ROBERT M B MACKENNA, London, England (by invitation) It was clearly shown in this case that the lesions are not present to any great degree

on the upper lid Epithelioma adenoides often attacks the upper lid, and adenoma sebaceum spares it

Contrast Sweating Above and Below Line of Paraplegia Presented by Dr T Cornbleet, Dr H Schorr and Dr N L Baker

H C, a Negro aged 25, was a patient at the Hines veterans' hospital from March 6, 1946 to January 1947 He complained of pain in the right leg and in the lower thoracic part of the spine, of four years' duration A laminectomy was done May 26, 1946, and a lesion was encountered at the level of the ninth thoracic vertebra which appeared to be an intramedullary cord tumor He was transferred to the Cook County Hospital Jan 20, 1947, where he complained of profuse sweating of the entire upper half of the body Injections of atropine sulfate afforded relief for two to three hours

Physical examination showed complete flaccid paralysis of the lower extremities Pain and pressure sense are diminished on the lower part of the abdomen and lower extremities There is no profuse sweating of the face, neck, upper extremities or trunk There are follicular keratoses of the sternum and other areas on the trunk

The urine contained albumin (1 plus) and many white blood cells The Kahn reaction of the blood was negative, and the blood cell count was normal The spinal fluid contained 330 cells per cubic millimeter, and the protein was 3,500 mg per hundred cubic centimeters

A roentgenogram taken after injection of opaque material indicated a complete block at the level of the ninth thoracic vertebra

DISCUSSION

Dr Stephen Rothman This is a good example of hyperhidrosis of organic central nervous system origin On the patient's back there are beginning signs of prickly heat, showing that softening of the horny layer and plugging of the pores occur in hyperhidrosis irrespective of whether it is peripheral or central in origin

Dr Theodore Cornbleet The patient presents all the changes in some areas that have been described for miliaria induced by heat Above the point of laminectomy and paraplegia there is excessive sweating, below there is excessive dryness The plugging of sweat pores and the changes that follow in miliaria are here reduplicated Thus it is excessive sweating itself which leads to cornification at the sweat duct orifices Heat is not necessary for the production of the syndrome, except in so far as it stimulates increased sweating

A Case for Diagnosis (Seborrheic Dermatitis) Presented by Dr Theodore Cornbleet and (by invitation) Dr D Cohen and Dr N L Baker

Cutaneous Blastomycosis, Therapeutic Result Presented by Dr F E Senear and staff

W S C, aged 57, was referred to the Department of Dermatology, Illinois Research and Educational Hospitals, in October 1946 with the diagnosis of blastomycosis, proved by biopsy Examination revealed an irregularly circinate plaque at the left commissure of the mouth, extending laterally on the cheek for about 8 cm The lesion was sharply marginated and had a precipitous border and a mammillated, somewhat elevated, crusted surface A few microabscesses were visible in the border, and the central portion of the lesion had healed, leaving a fine pinkish scar

CASE 2—B M, a nurse aged 29, had first noted approximately one year previously what was described as a pruritic, vesicular patch of dermatitis on the dorsal surface of her left hand It had occurred approximately ten hours after she had mixed penicillin solution, during which procedure a moderate amount of the concentrated solution had come into contact with the affected site During the next three months she had had several recurrences of pruritic, vesicular dermatitis on the dorsal surface of the hand, with complete remission between these episodes After this period, she had had more frequent attacks, as well as extension of involvement to the dorsal surface and sides of several fingers Furthermore, the lesions persisted between attacks, and at times superficial fissuring, which interfered with the movement of her fingers, occurred

Six months after the initial onset, all lesions cleared up completely during a three weeks' vacation, when the patient was away from her work as a clinic nurse There was prompt recurrence when she returned to work At this time she consulted a dermatologist, who found positive reactions to patch tests with penicillin, contact with this drug was discontinued There was slight improvement, but complete clearing did not occur, and the patient continued to have periodic exacer-

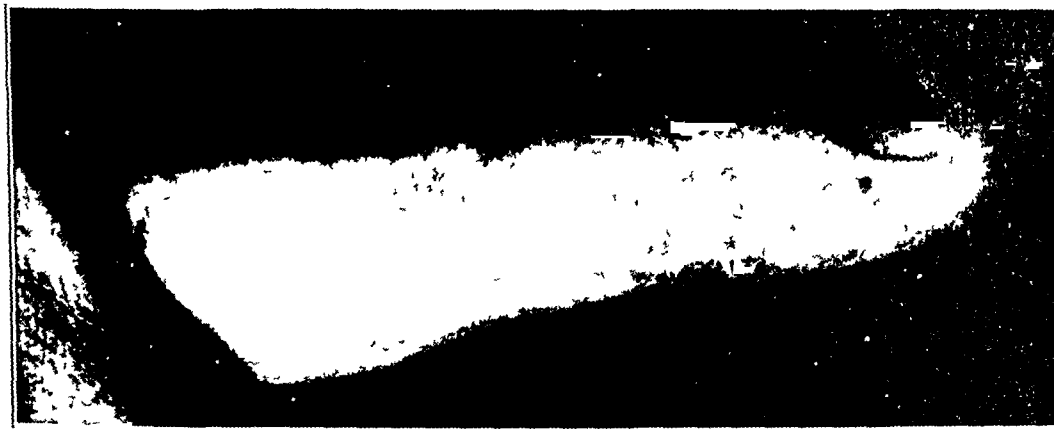


FIG 1 (case 2) —One of the eczematous plaques on the fingers, which on one occasion flared up simultaneously with the exacerbation of a lesion on the eyelid

bations Patch-testing was then done with procaine hydrochloride (novocain®) and streptomycin, with positive results, and therefore contact with these drugs was discontinued However, despite this action, during the next three months the patient continued to have repeated flare-ups, and finally it was necessary for her to discontinue her work for the second time Within one week, there was significant improvement, but she continued to have new vesicles and also had one distinct, rather severe exacerbation which was certainly not related to contact with penicillin, procaine hydrochloride or streptomycin At the time of the exacerbation she consulted an allergist, who confirmed the previously reported positive reactions to patch tests and also demonstrated that she had pronounced sensitivity to trichophytin, for this reason he advised a series of injections with trichophytin as an attempt at desensitization Because of financial reasons, it was essential for her to return to work There was no improvement, and indeed the severity and extent of her lesions gradually increased during the next two months, the exacerbations were not related to the injections of trichophytin

Other treatment included strict avoidance of soap and water, with use of a soap substitute, superficial roentgen therapy and application of several unidentified ointments

characteristic in that they are fairly well demarcated, erythematous, edematous and slightly scaling and in many respects resemble a fixed drug eruption

Individual lesions vary considerably In the vast majority of patients there is a vesicular element, although vesiculation may be absent There is a tendency to oozing and superficial fissuring, and in many persons vesicopustules and other signs of secondary pyogenic infections are dominant when the patient is first seen In general, the borders of plaques are not well demarcated, and they are not annular with a tendency to central clearing Pruritus, which is usually intense, is a regular feature of eczematous dermatitis due to food allergy The itching is periodic and varies from day to day unless one of the causative foods is eaten daily

When food diaries are used as a method of study, pruritus is almost as dependable as a sign of an exacerbation as is the appearance of new vesicles and other objective evidence

However, unfortunately, there are no absolute diagnostic criteria in distinguishing eczematous dermatitis due to food allergy from that due to other factors, but with experience it is possible for one to acquire a "high index of suspicion"

COURSE OF ECZEMATOUS DERMATITIS DUE TO FOOD ALLERGY

In most cases there is a history of a tendency to spontaneous exacerbations and partial remissions We have not been particularly impressed with a change of incidence in relation to the season of the year, although in general the process tends to be severer during the winter months

Quite uniformly, rapid, significant improvement has been noted in one to three days when the causative foods were eliminated, provided that the etiologic picture was not complicated by other factors, such as contactants and pyogenic infection Exacerbations which follow addition of an allergenic food have occurred within fifteen minutes after a small serving of a particular food, and, almost always, objective evidence of such exacerbations is preceded by pruritus On the other hand, the interval between ingestion and exacerbation has been as long as forty-eight hours after the food was eaten, and in 3 of our patients exacerbations did not occur until the food had been eaten on six consecutive days It seems quite certain that exacerbations occur more promptly and with a smaller quantity of the allergenic food if the addition to the diet is made within a few days after the initial lesions have become quiescent Many patients have been observed in whom decided prompt exacerbations occurred after ingestion of a given food soon after initial improvement had occurred on a trial diet, several weeks or months later, these same patients failed to have such exacerbations following the addition of the same food to the diet It would

When the patient consulted us, she had seven distinct, rather well demarcated, erythematous, oozing, scaling, vesicular plaques on the dorsal surface and sides of three fingers of the right hand, two fingers of the left hand and the right palm There was some crusting but no frank vesicopustules In addition, she had superficial fissures in several plaques, and there was some limitation of movment of the involved fingers The only other finding of importance was an erythematous, edematous, scaling, well demarcated plaque on the inner surface of the right upper eyelid The latter lesion had been noted about two weeks previously



Fig 2 (case 22) —The exacerbation which is illustrated followed the ingestion of smoked pork Concomitant bacterial infection was a complicating factor

The familial and personal allergic history were noncontributory except that the patient had had what had been diagnosed as allergic vasorhinitis on one occasion when she was living in Texas There was no history of any type of previous cutaneous disease or intolerance to any contactants encountered during her work as a nurse prior to the onset of her present trouble

The management and course of this patient's eczematous dermatitis during the seven months' observation period were as follows

1 She was advised to discontinue work, which she did for a three week period, and during this time Dr Norman Ingraham Jr did a complete allergy work-up,

seem that in many instances spontaneous desensitization takes place, and several months after disappearance of the patient's dermatitis foods which caused definite exacerbations previously may be taken without resultant symptoms or signs in the skin

Our experience is at variance with that of Rowe [7b] in that we believe that significant improvement is evident within several days to one week, provided that all the allergenic foods are eliminated from the diet and provided that all other contributory factors have been eliminated and treated Those patients who have other etiologic factors in addition to food allergy will not improve significantly on a therapeutic approach which is designed to find and eliminate only the food allergy factor

It is our opinion that the process in many of these patients had its onset as allergic contact dermatitis, and in others as a primary pyogenic dermatitis, for example Later on in the course of the disease, the specific food sensitivity factor became operative and in many instances became the chief perpetuating factor in the eruption Also, the reverse was true in that in some instances the eruption had its onset as an eczematous dermatitis due to foods and subsequently other factors, such as allergic contactants, invasion and sensitization by bacteria, complicated the process As in allergic contactant dermatitis it is advantageous for one to treat eczematous dermatitis due to food allergy early in the course of the disease because it is easier to effect a cure under these circumstances This point was well illustrated in many of our cases

INCIDENCE OF SENSITIVITY TO VARIOUS FOODS

This series of patients is too small for analysis as to the relative frequency with which individual foods may sensitize the skin, but it is interesting to tabulate the results for what they are worth In 1 or more patients the allergenic role of the following foods was demonstrated in our series of 26 patients, and in almost all instances exacerbations were noted on 2 or more occasions

Food	No of Patients	Food	No of Patients
Chocolate	9	Grapefruit	5
Sea food *	8	Tomatoes	4
Wheat	6	Eggs	4
Oranges	6	Broccoli	2
Pork	5	Rice	2
Milk	5	Cinnamon	2
Nuts	5	Smoked pork	2

* Lobster, 2, crab, 2, shrimp, 2, clams, 1, and shad, 1

Specific sensitivity to the following foods was encountered in 1 patient peaches, carrots, onions, peas, Scotch whisky, butter, veal, pepper, cauliflower, pimento, coffee, pineapple, tea, apricots, cabbage,

a summary of which follows Reactions to patch tests were negative for a long list of household and other contactants except for crystalline penicillin G (1 cc containing 25,000 units), 3 plus, a 2 per cent aqueous solution of procaine hydrochloride, 3 plus, and o'cedar® furniture polish (50 per cent in olive oil), 3 plus Scratch and intradermal tests with aqueous protein extracts of common dust-borne allergens, except for those with mixed feathers, sheep dander, rabbit hair and cow dander, had negative reactions Scratch tests with 140 foods had negative results except for weakly to moderately positive reactions to almonds, bananas, lima beans, Roquefort cheese, cherry, chicory, cinnamon, coconut, dates, grapefruit, milk, mustard, onions and poppy seed

2 She had about a 50 per cent improvement during the three week period when she was away from work, but she continued to have exacerbations characterized by intense pruritus and the appearance of new vesicles, particularly at the periphery of the involved sites At times, the eyelid lesion flared up concomitantly with the



Fig 3 (case 22) —This site of involvement had flare-ups on numerous occasions when one of the responsible food allergens was added to the diet The lesions on the patient's hand are illustrated in figure 2

lesions on her hands, but at other times either the eyelid lesion or the hand lesions flared up independently The only local treatment which was used consisted of aluminum acetate solution (1 20) soaks several times daily, followed by application of 3 per cent itchthammol in zinc oxide ointment After the allergy work-up, o'cedar® furniture polish was added to the list of contactants for her to avoid, and also the patient was asked to follow a diet consisting of only the foods which gave entirely negative reactions on scratch tests She returned to work, inasmuch as the severity of the exacerbations and their frequency during the time when she was away from work were such that the financial sacrifice did not seem justifiable

3 There was no significant improvement on a scratch test–negative diet during the next three week period, and therefore chocolate, coffee, orange, cheese and tomato and nuts were also eliminated from the diet, in addition, the patient was asked to keep a careful diet diary Wheat and eggs were not added to the list

string beans, lima beans, chicken, sweet corn, vanilla extract, rye, sweet potatoes, cheese, paprika and white potatoes At the present time another patient, for whom the primary food allergen is beef, is under observation, as is another, for whom canned pears are the most important food allergen

COMMENT

It should be emphasized particularly that, while allergic sensitivity to foods is an important reason for chronicity and persistence of an eczematous eruption, it is not an etiologic factor for even a majority of such patients, and study and treatment of the patient in this regard must be carried out with scrupulous regard for the many other possible etiologic factors concerned In addition, as with many other methods of treatment, too great enthusiasm or "faddism" for diets may have a medically deleterious effect on the whole patient Prolonged restriction of caloric intake, particularly for underweight patients, for many growing children or for the aged is obviously unjustified Likewise, the balance of various fractions in the diet and the adequacy of vitamin intake must receive thoughtful consideration Some patients will cooperate too enthusiastically for their general medical good and may continue to follow severely restricted diets for too long a time and with too little justification

In general, local treatment was not particularly helpful in the management of this series of cases, except in those in which bacterial infection was an important contributory factor Also, superficial roentgen ray therapy does not seem to influence significantly the course of eczematous dermatitis due to food allergy More than 50 per cent of our 26 patients had had an adequate trial of roentgen ray treatment, and, although apparent partial initial improvement had been noted in some patients, the end result was unsatisfactory in all cases in that relapse occurred within a short time after the treatment was discontinued Penicillin administered parenterally was useful in controlling pyogenic infection when this was a complicating factor

The history in regard to food sensitivities and other allergic manifestations prior to the onset of the presenting dermatitis was not particularly helpful in the initial evaluation of these patients There was a family history of allergy for 15 per cent of the patients and a personal allergic (not atopic dermatitis) history for 15 per cent, although the two groups were not identical

The psychogenic factor seemed to be important for several of our patients, and indeed our experience with the present series leads us to believe that there is an emotional component in the background of the vast majority of persons with food sensitivities For this reason, one must be careful to evaluate each patient critically and include in the

of foods to be eliminated at this time because it is most difficult for one to avoid these foods in a hospital dining room

4 The patient had some improvement in her condition in the next two weeks, but continued to have periodic flare-ups, although they were less severe than previously At this time wheat was added to the foods to be eliminated from the diet

5 There was no change in the next week, and at this time it was decided to add eggs to the interdicted foods, which action meant that the total restriction of the diet included the elimination of almonds, bananas, lima beans, Roquefort cheese, cherries, cinnamon, chicory, coconut, dates, grapefruit, milk, mustard, onion and poppy seed, which had been eliminated on the basis of positive reactions to scratch testing, and chocolate, coffee, orange, cheese, tomatoes, nuts, wheat and eggs, which had been eliminated in an effort to obtain a so-called basic nonallergenic diet

6 During the next two weeks, after the elimination of eggs from the diet, there was more sustained improvement than at any previous time since the patient had come under our observation, and for the first time there was complete absence of pruritus and no appearance of new vesicles within the last week

7 Five days later the patient had a distinct flare-up at all previously involved sites, including the eyelid, characterized by pruritus, vesiculation, oozing, erythema and edema This exacerbation occurred approximately six hours after she had eaten one boiled egg It subsided entirely within five days

8 After this development, the patient remained free of symptoms and lesions except for four exacerbations, all of which subsided promptly The first such exacerbation did not occur until she had eaten one egg daily for three days, the second, until she had eaten one egg daily for six days, and the third, until after she had increased her intake of milk to one quart daily for three consecutive days During the next six weeks all other interdicted foods were added, without any exacerbation, so that, at the end of this time, the restriction of her diet included only the elimination of eggs and the limitation of milk to one glass daily, with no restriction of foods containing milk

9 During the next three months her hands and eyelid remained clear, despite the addition of all foods containing eggs to her diet, although she continued to restrict eggs to three weekly (one every other morning for breakfast) She had continued to work as a nurse and had done all her own housework, with avoidance of furniture polish, procaine hydrochloride, penicillin and streptomycin, but with no other restrictions or precautions

The diagnosis was eczematous dermatitis of the hand and left eyelid, due to allergic contactants (penicillin, streptomycin, procaine hydrochloride and o'cedar® furniture polish) and food allergy (eggs and milk)

Comment It seems apparent that this patient originally had an allergic contact eczematous dermatitis and that the food allergy factor did not enter the picture until approximately six months after the onset of her dermatitis, which gradually increased in severity, presumably because of repeated exposure to the allergic contactants It is obvious that the responsible foods would have been discovered promptly if this patient had been hospitalized or if a resrticted elimination diet had been put into effect early in our observation period When egg was added to the diet one week after pronounced improvement had occurred, a

group of persons with food allergy only those patients who have definite repeated exacerbations following the addition of causative foods to the basic diet It is conceivable that at least some of these patients could be cured with ideal psychiatric treatment, but this approach has had limited usefulness in our experience This principle was illustrated in the case of 1 patient who had repeated exacerbations of her dermatitis after the ingestion of small quantities of grapefruit during a period of considerable emotional strain incident to working under an exacting employer, some months later, under more favorable circumstances of employment, it was possible for her to eat several times as much grapefruit with only minimal pruritus and very few objective signs of involvement

It is essential for one to realize that there is an appreciable individual variation in the course of patients who have eczematous dermatitis entirely or in part due to specific food sensitivity In some cases a prompt regression of the dermatitis is noted after the interdiction of the responsible foods, in others significant improvement does not occur for as long as seven to ten days The same variation applies to the onset of an exacerbation following the addition of a causative food, although in the vast majority of cases such exacerbations are seen within a period of forty-eight hours It is not a simple procedure to manage the patients successfully, and considerable experience is necessary before one acquires an appreciation of the problems involved The physician who follows a stereotyped approach will not cure a significant percentage of patients with cutaneous food allergy

SUMMARY AND CONCLUSIONS

1 A series of 26 patients with eczematous dermatitis, for whom it was demonstrated that specific sensitivity to various foods was the only etiologic factor or a significant contributory factor, is presented

2 The chief localization site encountered was the hands (involved in 81 per cent), although the feet, eyelids, legs, arms, face, scrotum, groins, neck, buttocks, perianal region and axillas were also involved in 1 or more of our patients

3 In addition to food allergy, other concomitant etiologic factors, including allergic contactants, primary irritants, pyogenic infection and pyogenic sensitization and allergic drug factors, were demonstrated for 12, or 46 per cent, of these 26 patients

4 Eczematous dermatitis due to food allergy tends to occur in localized, rather inflammatory plaques, oozing, vesiculation and excoriations were noted in a high percentage of cases Apparent spontaneous exacerbations and partial remissions are relatively common

5 Pruritis, which was usually quite severe, was a regular and prominent feature of the process

flare-up ensued within a short time after the ingestion of only one egg, six weeks after the lesions had become quiescent, a flare-up did not occur until the patient had eaten one egg daily for six consecutive days, several months later, she was able to eat three eggs weekly, as well as foods containing eggs, without any return of pruritus or objective signs This spontaneous desensitization is a common sequence of events, provided that all causes of the eczematous dermatitis have been eliminated and the lesions have remained entirely clear for several weeks to several months It may be noted that she had a negative reaction to a scratch test with the only significant food allergen which was one of the proved causative factors



Fig 4 (case 11) —The patient also had large, oozing, eczematous plaques on both legs Numerous exacerbations such as the one illustrated were demonstrated on the addition of wheat and chocolate to the diet

Case 3—H H, a secretary aged 36, was referred to us because of an unusually severe, patchy, eczematous dermatitis of the feet and hands, with maximal involvement of the feet, which had been present for fifteen months This was characterized by scaling, erythematous, superficially denuded, crusted, vesicular, fissured plaques on the inner surface of the right foot, extending from the instep to the dorsal surface of the foot and involving part of the ankle, the dorsal surface of the right foot at the base of the first interdigital space and extending into the interdigital space, the instep of the left foot and the medial surface of the left foot just above the heel The borders of the lesions were not well demarcated, only a few vesicles were seen In addition, there was a faintly erythematous, rather well demarcated, dry, slightly lichenified plaque on each palm, as well as a few superficial vesicles along the sides of several fingers All lesions tended to be dry, scaly and somewhat lichenified rather than oozing, although there was some exudation at several sites on the feet

6 Scratch tests with foods were of almost no value in the management of these patients

7 The methods of approach in the study of these patients are discussed in some detail Ideally, the vast majority should be hospitalized for an adequate evaluation from the standpoint of food allergy, for about 40 per cent of our patients such evaluation would not have been possible without hospitalization However, with a fair percentage of cooperative patients, satisfactory elimination diets can be put into effect on an outpatient basis, especially if food allergy is the only etiologic factor involved

8 The necessity of evaluating and treating such patients along broad etiologic lines as well as with respect to food allergy is emphasized and illustrated in the case histories of many of our patients

9 Chocolate, oranges, wheat, pork, eggs, sea food, tomatoes, grapefruit, nuts and milk were encountered more frequently as food allergens in this series of patients, but specific food sensitivity was demonstrated to twenty-six other foods by one or more patients Sensitivity to two or more foods was demonstrated by 24 of the 26 patients

10 It is believed that food allergy is one of the important etiologic factors in eczematous dermatitis In our experience, food allergy is the only etiologic factor or a significant contributory factor in the case of 16 to 18 per cent of patients with chronic eczematous dermatitis of the hands and/or feet

11 The technic of management and interpretation of results are relatively difficult, especially in the cases of those patients for whom food allergy is only one of numerous possible etiologic factors

Department of Dermatology, University of Texas School of Medicine

133 South Thirty-Sixth Street

ABSTRACT OF DISCUSSION

DR SAMUEL M PECK, New York I wish to congratulate Dr Livingood for the fine piece of work which he did and especially for his patience in carrying out this type of rather ungrateful research The average dermatologist is somewhat prone to disregard the value of the approach which Dr Livingood has made because, on the one hand, it is so time consuming and, on the other, the results in many instances are most disappointing I think the chief difficulty in this problem is the fact that one is unable to judge on clinical evidence alone which cases are due to foods and which are due to the many other factors which can give the same clinical syndrome Also, it is very rare to have a factor such as food sensitivity play other than a major or a minor role in the dermatitis Food plays a role in infancy and childhood as the sole cause of eczema This point no one will deny However, it is difficult for many to visualize a dermatitis which is limited to the hands as being mainly due to a food factor Certainly, in the eczema of infancy and childhood, one rarely, if ever, sees limited localization, especially as far as the hands are concerned It would be a great help if there

This condition had had its onset as a rather small, coin-shaped, pruritic, scaling, eczematous plaque on the inner surface of the right foot, approximately fifteen months before the patient consulted us Soon afterward, there had been progressive extension and increase of pruritus, which was intense and occurred in paroxysms The course had been characterized by repeated exacerbation and partial remission, but complete clearing had not occurred at any time, and pruritus had not been absent for more than one or two days at a time The patient had been under the care of a radiologist, who had given her approximately fifteen roentgen ray treatments, during which course of therapy she had had partial improvement and one lesion which had appeared on the flexor surface of the wrist had disappeared



Fig 5 (case 24) —In some respects case 24 was one of the most interesting in our series despite the apparent insignificance of the involvement The lesion resembled a fixed drug eruption It had persisted for almost three years and disappeared within seven days after the responsible food allergens were eliminated Numerous prompt exacerbations were demonstrated on the addition of food allergens to the diet

entirely She had received a total of 1,500 r to all affected sites Soon after the roentgen ray treatments were discontinued, there had been progressive increase of involvement, and for this reason the radiologist had referred her to us The management and the course of her eczematous dermatitis during the twelve month period of observation were as follows

1 Hospitalization was strongly advised, but this was not possible All previous local medication, which had been quite varied, was discontinued, and 3 per cent

were a simple approach to establish or rule out foods as etiologic factors I have attempted to find one in many instances, but so far, the necessary procedure still boils down to the tedious, long-drawn-out, trial and error type of approach One thing should be emphasized, namely, that, as I believe, in different parts of the country and probably among different classes of population different combinations of factors are responsible for the dermatitis on the hands In the few cases in which I believe I have definitely established food allergy as a cause of eruptions on the hands, nearly all the patients were females If this observation is common, I think it should be helpful Furthermore, when a patient with a dermatitis on the hands presents himself or herself to me, I automatically lean away from consideration of food as an etiologic factor in the dermatitis of the hands in men, for them fungi, bacteria and contact factors are the predominating etiologic agents In women, bacteria or molds will also play a role if the eruption is present long enough I should like to cite 1 case which to me was enough payment in satisfaction and compensated for all the failures with this approach This was of a young married woman who came to me with a dermatitis of the hands of months' duration I automatically went through the routine procedures of looking for an infectious agent and for household contacts as the cause of her dermatitis I totally disregarded the fact that I had treated her successfully for food allergies as the cause of her infantile eczema In looking over her old records, I found mention of this, and when she eliminated the foods to which she had again become sensitive over the years, the dermatitis on her hands finally cleared up One must bear in mind that, even when the offending foods are removed, there is no dramatic improvement Patience and a thorough understanding of all the factors which contribute to the dermatitis are all needed in order for one to treat one of these patients successfully I wish to congratulate Dr Livingood and Dr Pillsbury for an excellent paper

Dr Earl D Osborne, Buffalo I, too, wish to congratulate Dr Livingood and Dr Pillsbury on having cured anyone with a condition having a food factor in an allergic background It is a very difficult job to undertake There are a few observations I should like to make First, I do not believe that it has been proved that protein substances as such will produce eczematous reactions When one speaks of foods, one must realize that one is talking about a very chemically complex subject Foods contain not only proteins but also fats, carbohydrates and a multiplicity of oleoresins I should like to ask Dr Livingood whether he did any patch testing in his cases with oleoresins present in the various foods It appears to me that it is possible for one to explain many apparent recurring vesicular eruptions of the hands on the basis of the ingestion of specific oleoresins present in various foods It is known that in the case of poison ivy and other weed dermatoses a flare-up of a preexisting eruption on any part of the body can be produced by the ingestion of the specific or related oleoresin concerned I believe that specific hypersensitivity does exist to the oleoresins in many fruits and vegetables, both from local contact and, in recurrences following this, from the ingestion of the specific oleoresin Finally, it is my belief that investigation will show that when foods are at fault in the production of an eczematous eruption the responsibility is probably that of the oleoresin content and not of the protein, carbohydrate or fat content of the particular food

Dr Eugene F Traub, New York I, too, enjoyed Dr Livingood's presentation and wish to thank him I should like to ask him several questions Were the cases in which the condition appeared to be influenced by or to react to certain foods discovered through the use of test diets, or did the patients react positively to tests with food to which they were not otherwise known to be sensitive? What

ichthammol in zinc ointment was prescribed A summary of an allergy work-up, done by Dr Norman Ingraham Jr, follows

A Patch tests of a wide variety of contactants, including eight different constituents of her shoes, and nylons, had entirely negative reactions

B Reactions to scratch and intradermal tests with common dust-borne allergens were completely negative

C A number of sharply positive reactions to scratch tests with foods were obtained, and it was Dr Ingraham's opinion that these were of a type which would



Fig 6 (case 4) —There was an important contributory pyogenic factor in this patient's eruption, and evaluation of the food allergy factor was not possible until the bacterial infection was treated concomitantly

make one feel that they could be of significance The foods producing positive reactions were almonds, apples, asparagus, bananas, beets, broccoli, carrots, cashew nuts, cauliflower, American cheese, Roquefort cheese, cherries, cinnamon, coconut, coffee, dates, dill, eggplant, lemons, mushrooms, oats, oranges, peanuts, white potatoes, prunes, spinach, turkey, watercress and wheat During this two week period there was no restriction of the patient's diet and no improvment

2 Within one week after she was placed on a scratch test–negative diet, there was 75 per cent improvement in all lesions, with decrease of pruritus Two weeks

was the percentage of cases in which skin tests with food were helpful? Did any adults in the series that were found to be sensitive to food give any history of having been previously sensitive to that particular food, or had they always enjoyed that food in the past? How long did this newly discovered food sensitivity last? Was it permanent, or did it clear up after the other factors had been removed?

DR MARION SULZBERGER, New York I wish to compliment Dr Livingood and Dr Pillsbury on an excellent paper The first point I should like to emphasize is that no one who has not attempted to carry out exact diets on ambulatory patients can realize how difficult the task is My own results with this method in the last fifteen years have been on the whole very unsatisfactory I should like to point out that it is almost prohibitively difficult for the patient to carry out a rigid elimination diet While on such diets the patient can join in almost no social activities—no eating out, no lunches while away from home, no participation in meals with others and no snack or candy or drink between meals, for example I have found that under these conditions patients either make involuntary slips or keep cheating The second point I should like to stress is that it is now obvious that atopic dermatitis has an eczematous phase This is true, not only in infants but in adults, although in the latter it is not as uncommon This form of atopic eczematous eruption may, of course, be susceptible to flare-ups following exposure to allergenic foods, just as are some cases of infantile eczema And in adults atopic eczematous eruptions can and do appear on the hands, particularly the dorsa of the fingers

Did Dr Livingood exclude the external contact with foods? It is difficult for one to eat bread or oranges, for example, without letting them touch the hands I think that in order to come to the conclusions that these eruptions are due to ingestion of foods, one must always and absolutely exclude the possibility of external contact, and I feel certain Dr Livingood has done this

I enjoyed the presentation and should like to suggest that Dr Livingood and Dr Pillsbury may in the future find it advantageous to attempt to classify their cases of "hand eczemas" into two large groups, namely, those of nonatopic and atopic dermatoses

My impression is that the results following elimination of certain foods would be much greater in atopic persons than in the nonatopic ones Moreover, for reasons which I mentioned in discussing aberrations of sweating, the role of foods and drugs in exacerbations of dyshidrosis may merit careful scrutiny in the future

DR CLARENCE S LIVINGOOD, Philadelphia I wish to thank the discussers Many of the questions brought up in these discussions are answered in our paper In answer to the questions of Drs Sulzberger and Osborn, with reference to external contact with food, rather than ingestion, as a factor We had thought of that point, and it has been our experience that eczematous lesions in some cases are caused by contactant sensitivity to foods, especially citrus fruits and vegetables However, in our series of cases, external sensitization to foods was a minor factor in comparison with endogenous allergy to foods We have been careful in evaluating this particular question, and, for example, in some cases suspected foods were given in capsule form

The duration of sensitivity to a particular food or foods varies in individual cases In some of our cases the sensitivity disappeared within several weeks after the lesions had disappeared, in others repeated exacerbations could be reproduced as long as six to eight months after the involution of the eruption, and in some it is probable that the sensitivity persists indefinitely We agree with Dr Peck that the allergic pattern in regard to food sensitivity in a given case is likely to change over a period of years

later, there was no additional improvement Therefore, she was asked to try for one week a basic "nonallergenic" diet consisting only of apricots, peaches, canned pears, prunes, sugar, tea, beans, chicken, string beans, lamb, lettuce, cabbage, peas, ry-crisp,® corn bread, salt, sweet potatoes, turnips, peach preserves and apricot preserves After one week on this diet, she had complete relief of pruritus and all signs of involvement, except for residual hyperpigmentation, scaling and very slight lichenification, had disappeared

3 At this time, she went on vacation and disregarded her diet entirely On successive days, she ate sea food dinners and chocolate candy—indeed, there was no interdiction of foods Within twelve hours after the first such meal, there was pronounced recurrence of pruritus, followed by a sharp, severe exacerbation involving all previously affected sites During the next three weeks, she resumed her scratch test–negative diet except that chocolate, nuts and all sea foods were added to the interdicted foods The pruritus disappeared within three days, and regression of objective signs gradually occurred except for one exacerbation possibly associated with the ingestion of watermelon At the end of three weeks, the patient was free from pruritus, and only residual hyperpigmentation and slight scaling persisted at the previously involved sites

4 During the past eight months, this patient noted repeated exacerbations following the attempted addition of the following foods to her diet wheat bread, or wheat flour in any form, chocolate, shrimp, crab meat, lobster and coffee In the last three months, she has been able to drink an occasional cup of coffee without exacerbation except for transient pruritus She has found that complete elimination of wheat products for a period of two or three weeks, as well as interdiction of chocolate, shrimp, crab, lobster and coffee, is followed by complete absence of all signs of involvement Furthermore, if the ingestion of wheat products is limited to two pieces of part rye and part wheat bread daily, pruritus and scaling of previously affected sites are so minimal that they do not interfere with any of her activities, therefore, she prefers to accept these consequences rather than eliminate bread entirely Repeated attempts to increase the amount of wheat-containing foods resulted in decided increase of pruritus of the eczematous patches at approximately the original sites of involvement

The diagnosis was eczematous dermatitis, due to food allergy (wheat, chocolate, coffee, shrimp, crab and lobster), of the hands and feet

Comment The initial elimination diet, which was based on scratch test–negative foods, happened to exclude the principal food allergen, which was wheat, and, also, it resulted in the interdiction of coffee, which was a relatively unimportant food allergen Complete improvement did not occur on this dietary regimen because of other specific food sensitivities in the form of several different sea foods and chocolate, all of which produced negative reactions in scratch tests Complete relief of symptoms and disappearance of pruritus followed a brief period of pronounced dietary restriction, which happened to exclude all the responsible food allergens It is probable that this patient could have been cured by a brief period of hospitalization and the use of a strict trial diet The rapid response to interdiction of foods would have made it possible to add foods rather rapidly, and within one month she could have been placed on a quite adequate diet

TRAUMATIC MARGINAL ALOPECIA IN WHITE WOMEN

SAMUEL AYRES Jr, M D
SAMUEL AYRES III, M D
AND
JOSEPH I MIROVICH, M D
LOS ANGELES

COSTA and Junqueira[1] recently summarized the literature on traumatic marginal alopecia, which, according to their observations and those of Ribeiro,[2] occurs almost exclusively in Negro and mulatto women They pointed out the similarity between this condition and alopecia liminaris frontalis as described by Sabouraud[3] and expressed the opinion that both conditions are caused by stretching the hair in tight braids or "buns" and, especially in the case of Negro women, by efforts to straighten kinky hair Folliculitis frequently results from this constant traction, and, with or without folliculitis, atrophic changes of the follicles gradually develop and lead to permanent alopecia

In the cases described by Ribeiro and by Costa and Junqueira the alopecia occurred in triangular areas involving the temples, with the apex pointing downward in front of the ears

Inasmuch as the previously reported cases of this entity occurred exclusively in Negro or mulatto women, except for 1 case in a white woman, mentioned by Ribeiro, it seemed worth while to record 5 cases in white women

In view of the fact that the alopecia tends to be permanent if the trauma due to traction from tight hairdress or excessive brushing is allowed to continue, it becomes important for one to recognize the

1 Costa, O G, and Junqueira, M de A Traumatic Marginal Alopecia Due to Traction on the Hair A Comparative Study of Alopecia Liminaris Frontalis of Sabouraud, Arch Dermat & Syph **48** 527-532 (Nov) 1943

2 Ribeiro, H Alopecia marginal traumatica por tracção dos cabellos, Brasil-med **52** 1267-1271, 1937, Alopecie marginale traumatique, Ann de dermat et syph **9** 495-503, 1938

3 Sabouraud, R, in Darier, J, and others Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, pt 7, p 13, De l'alopecie liminaire frontale, Ann de dermat et syph **2** 446-460, 1931, Diagnostic et traitement des affections du cuir chevelu, Paris, Masson & Cie, 1932, p 398, Pelades et alopecies cicatricielles, ibid, 1929, p 93

SUMMARY STUDY AND TREATMENT OF PATIENTS

The successful study and treatment of these 26 patients from the food allergy point of view was accomplished by the following methods (1) strict trial diet including hospitalization, for 11 patients, (2) basic "nonallergic" diet, for 9 patients, (3) "spot" elimination diet, for 5 patients, and (4) scratch test–negative diet, for 1 patient

Furthermore, attention to other factors, including careful study and elimination of contactants and primary irritants, elimination of the use of drugs (internal) in several patients, and treatment of the pyogenic factor, was necessary in 12 of the 26 patients Cure was obtained in only 54 per cent of these 26 patients by determination and elimination of the responsible food allergens alone

At the same time, it is emphasized that food allergy was such an important contributory factor in the disorders of the other 46 per cent of the patients in whom it was not the only etiologic factor that a satisfactory therapeutic result could not have been accomplished without the discovery and elimination of the allergic foods

From these data, it would seem that any single dietary method of approach, without consideration of other factors, will result in misconception with regard to the possible primary or contributory food sensitivity factor, and resultant therapeutic failure In those patients in whom a food sensitivity is the only etiologic factor, prompt improvement and a clinical cure will follow the institution of a suitable elimination diet We agree with Flood and Perry that the strict trial diet will result in the highest percentage of cures, but the basic nonallergenic diet which we have used on an outpatient basis will be effective for a significant number of patients for whom food allergy is the only etiologic factor The so-called "spot elimination diet," which simply provides for the interdiction of a small number of foods of high allergenic index, will effect a cure in a fairly small percentage of patients The failure of any particular dietary regimen tends to discourage the patient and makes it difficult for one to institute a more rigid dietary approach In general, it is preferable for one to outline a diet which informs the patient what he is to eat, rather than one which tells him what he is not to eat In the other large group of patients, in whom food sensitivity is only a contributory concomitant factor of varying importance, study and treatment is much less rewarding therapeutically, without hospitalization, it is most difficult for one to untangle and treat the multiple etiologic factors involved

INCIDENCE OF FOOD ALLERGY IN ETIOLOGY OF ECZEMATOUS DERMATITIS

It is difficult for one to evaluate accurately the role of food allergy in the etiology of eczematous dermatitis so far as the exact incidence is concerned In the first place, it is not possible for one to exclude food

entity and to advise regarding corrective measures After atrophy of the follicles has taken place no method of treatment would be likely to succeed If the causative factors are eliminated early enough, complete recovery takes place, according to the aforementioned observers

REPORT OF CASES

CASE 1—D H, a girl aged 18, came in primarily for the treatment of acne of a moderate degree of activity In addition to the acne examination revealed a pronounced thinning of the hair along the sides of the scalp above the ears, where the hair was pulled up toward the top of the head in tight braids Scattered through the areas of partial alopecia were a number of small follicular papulopustules

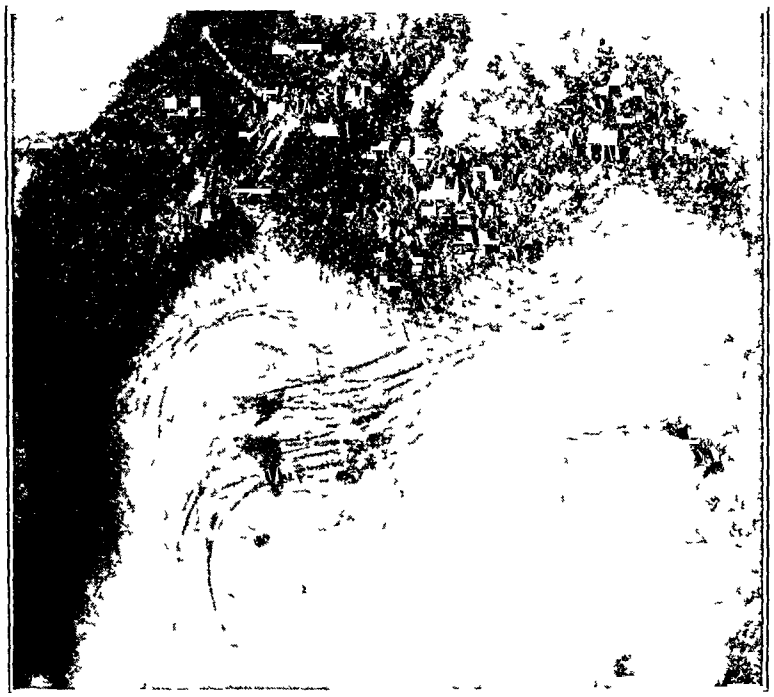


FIG 1 (case 1)—Area of alopecia in front of and above ear, due to constant traction from tight braids

CASE 2—A C, a girl aged 18, came to the office primarily for the treatment of redness, crusting and slight swelling of the eyelid margins, characteristic of blepharitis Examination revealed, in addition to the condition of the eyelids, a moderate degree of thinning of the hair on both temple areas in front of the ears There were a number of broken hairs, some of them with an exclamation point appearance, and a few follicular pustules scattered through these areas The patient had been in the habit of using metal curlers on the sides of her scalp for the preceding four months She thought that the thinning of the hair was of about six weeks' duration

CASE 3—E W, a woman aged 65, presented herself with a complaint of an eruption on the sides of the scalp, associated with a thinning of the hair which had been present for about six months The patient had been using metal curlers at night

allergy as an etiologic factor in a given case unless the patient is hospitalized and placed on a strict trial diet and unless there is the elimination of other possible contributory factors, such as pyogenic infection and contactants, which might obscure a concomitant food sensitivity Obviously, such a procedure is not feasible in a fair percentage of cases Furthermore, the experience of various investigators will differ considerably For example, physicians in industry will encounter a higher incidence of eczematous dermatitis due to allergic contactant and primary irritant factors It has been our experience that food allergy is the only significant etiologic factor for about 7 to 8 per cent of the patients with chronic eczematous dermatitis and an important contributory factor for an additional 8 to 10 per cent of such patients The common concomitant factors which were recognized in the present series of 26 patients include allergic contactant, primary irritant, pyogenic infection and sensitization and drug allergy

DESCRIPTION OF LESIONS

We agree with Sulzberger that if food allergens cause eczematous eruptions of the hands "then foods must be considered as possible etiologic agents in other eczematous eruptions no matter what their localization", and it has been our experience that such eruptions due to specific food sensitivity do occur at other sites on the cutaneous surface

We have recorded the following sites of involvement in one or more patients all surfaces of the hands and feet, the eyelids, the forearms, the upper arms, the legs, the thighs, the face, the neck, the groins, the posterior surface of the scrotum, the axillas, the external auditory canals, the trunk and the buttocks It is true that the hand is the site of predilection, but this is certainly not the only site of localization In our series of cases, the hands were involved in 21 of 26 patients, the dermatitis was limited to the hands with no other involved sites in only 10 of the 26 patients

Eczematous dermatitis due to food allergy tends to be patchy rather than diffuse The dorsal surface and sides of the fingers, the palms, the dorsal surface of the hands and the interdigital spaces occasionally have been sites of localization which we have noted on the hands On the feet, the patches tend to be localized on the inner and dorsal surfaces of the feet, although the distribution may be on the dorsal surface of the toes, suggesting an allergic contact dermatitis, or on the plantar surface of the feet, suggesting dermatophytosis Usually the involvement is in the form of plaques, although patients with diffuse involvement of the axillas and groins, as well as with diffuse involvement of the extremities, have been observed The eyelid lesions are quite

Examination revealed a diffuse thinning of the hair over the scalp, with a mild seborrheal scaling Involving each temple area in front of the ears there was a more pronounced loss of hair, with a few broken hairs and empty follicles Just above this area on both sides was a transverse erythematous and slightly elevated ridge or streak which the patient stated coincided with the area covered by the metal curlers There were a few follicular papules in this erythematous area A patch test with the patient's aluminum curler gave no reaction

CASE 4—D H, a girl aged 11, had noticed thinning of the hair, with irritation along the temples, for about two weeks The patient had been in the habit of rolling her hair tightly with metal curlers at night and had been spending a great deal of time every day brushing her hair upward along the sides

Examination revealed a moderate degree of thinning of the hair along the temples in front of and just above the ears There were a number of broken



FIG 2 (case 3)—Triangular area of alopecia involving the temporal region in front of the ear due to constant traction from the use of tight curlers

hairs, one of which was shaped like an exclamation point There was also a moderate degree of redness on each side of the scalp and a number of small superficial papules, several of which were crusted A patch test was made with nickel, but the patient did not return for observation

CASE 5—E J S, a woman aged 30, had had a scalp disorder for one and a half years The patient had been in the habit of combing and brushing the hair upward from the sides and fastening it in a tight braid

Examination revealed an appreciable thinning of the hair, with some erythema, over the temporal regions Some of the empty follicles showed dark plugs, and there was evidence of atrophy throughout the areas

Roentgen irradiation, in a total dose of 2,085 r, has been administered, along with potassium iodide orally in a maximum daily dose of 90 minims (about 6 cc) The lesion has cleared except for four small crusted areas at the periphery

Blastomycosis Presented by DR EDWARD A OLIVER and DR J M MCCUSKEY

The patient is a dairy operator and handles powdered milk The lesions appeared about four weeks ago

At present there are twelve nodular lesions on the face and the back of the neck, varying in size from that of a split pea to that of a hazelnut The lesions are erythematous, boggy and studded with pinpoint to pinhead-sized yellow pustules, especially at the periphery On the right hand, there is a deep, erythematous, indurated mass, the size of a hen's egg

Microscopic examination of material from the periphery of the lesions showed Blastomyces

DISCUSSION OF PREVIOUS TWO CASES

DR OLIVER S ORMSBY Years ago, when we had foreign guests, it was possible within a short period to bring in several patients with blastomycosis for demonstration Such cases are now comparatively rare There was a time when I had 100 cultures grown from 100 different patients Dr MacKenna can get no idea about what blastomycosis looks like by seeing the patients presented today One patient was cured with efficient treatment, and the other did not have typical lesions The skin lesions in a typical case are classic They occur in plaques with elevated margins and a superficial smooth scar in the center The margin of the lesion slopes and contains true abscesses in which Blastomyces are found The cases of systemic disease are different My co-workers and I had the privilege of reporting the first one in 1903, in which the lesions were clinically and symptomatically blastomycosis The lesions in that case consisted of subcutaneous abscesses, ulcerations and nodules We proved that the skin lesions came by way of the circulation At that time a large number of patients with systemic blastomycosis died—at least 50 per cent of the patients with systemic disease died The course was like that of severe pellagra some years ago I was in London when the disease was being discussed in this country, and the London men were much interested It was not until 1907, when many physicians from abroad were here to attend the international congress, that we were able to demonstrate to our foreign guests that blastomycosis was an entity—they thought it was syphilis I am sorry that Dr MacKenna did not see an example of the American variety of the disease

DR STEPHEN ROTHMAN We will have the opportunity to demonstrate a case of extensive American blastomycosis to Dr MacKenna tomorrow in Billings Hospital Dr Senear's patient has shown remarkable response to therapy In cases with widespread lesions the initial therapeutic effect of iodides is always impressive, but it takes years for them to clear up The lesions heal rapidly in the center but spread peripherally The supporting effect of local roentgen irradiations is rather modest Local application of fungicides is ineffective, in spite of their fair fungicidal action on Blastomyces in vitro We have not seen any beneficial effect of vaccine therapy Apparently cases with small simple lesions are easier to manage

DR. M J REUTER, Milwaukee In Dr Senear's case there is still some activity around the borders of the lesions In resistant plaques such as this, I

have been destroying the lesion with diathermy, at the same time giving the patient large doses of potassium iodide by mouth

DR THEODORE CORNBLEET The surgeons think that the dermatologists' approach to the treatment of cutaneous blastomycosis with medical measures is inadequate, inefficient and a loss of time They believe, at least some of them, that the lesions should be excised and the defects grafted They believe that even large areas are better treated with such a direct attack Their view is that as long as the disease is superficial breadth of area involved is a secondary consideration

DR FRED BECKER, Duluth, Minn Some investigators have expressed the belief that, prior to iodide therapy for systemic blastomycosis, a cutaneous test with a Blastomyces vaccine should be performed If the result is positive, it denotes allergy and desensitization must be performed, with gradually increasing doses of the vaccine until this positive cutaneous sensitivity is eliminated Then only should iodine therapy be instituted They cited several cases in which giving iodides produced rather disastrous results in a patient highly sensitive to the vaccine

DR STEPHEN ROTHMAN I understood that vaccine was required as initial therapy in cases with hypersensitivity to iodides and that the vaccine therapy was supposed to desensitize to iodides I wonder whether these observations have been corroborated In our case with no iodide sensitivity, vaccine therapy had no effect whatsoever although the patient shows strongly positive cutaneous reactions to the vaccine

DR ADOLPH ROSTENBERG JR (by invitation) I have had no firsthand experience treating blastomycosis As I understand Conant and his colleagues, a patient with systemic involvement who is allergic to a blastomycosis vaccine may have a spread of the blastomycosis if he is given iodides If the vaccine is given first some kind of immunity develops, so that the patient is subsequently able to take iodides The present immunologic point of view regarding diseases such as blastomycosis has altered considerably Primarily through the work of Dr Rich at Johns Hopkins Hospital it has been realized that there is dissociation between so-called immune phases and the hypersensitive phases of a disease and not, as originally stated, that hypersensitivity is a way station on the road to immunity This makes it questionable whether anything is accomplished from the point of view of immunity by desensitization in the tuberculin type of sensitization Possibly one succeeds only in abolishing or reducing the skin reaction

DR F E SENEAR Dr Ormsby recommended that arsphenamine therapy be employed when patients who had been receiving iodides for blastomycosis failed to show further progress and that after this procedure, with the use of but a few injections, the blastomycosis would again become responsive to iodide therapy

While I believe that American blastomycosis is not seen as frequently now as in the past, there has been a change in the clinical appearance of this disorder My co-workers and I have recently seen several patients with cutaneous manifestations from systemic blastomycosis, and in these instances a considerable number of widely scattered lesions have developed spontaneously About three years ago, I had, in the space of four months, 3 patients in this category The organism is readily demonstrable in lesions of this type We have also seen in recent years a larger number of patients with the deep-seated furunculoid, or cold abscess, type of lesion

SUMMARY

Five cases are reported of traumatic marginal alopecia in white women

The clinical appearance consists of a triangular area of partial alopecia involving the sides of the scalp above or in front of the ears, usually accompanied by folliculitis and atrophy of the follicles

The condition is believed to be caused by persistent traction on the hair from vigorous and prolonged brushing, a tight hairdress or the use of curlers Previously reported cases of this condition have occurred in Negroes or mulattoes

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5 T gypseum was identified as the etiologic agent in about two thirds of the cases of tinea pedis yielding cultures and in about 60 per cent of the cases of tinea unguium yielding cultures T rubrum was identified as the etiologic agent in two thirds of the cases of tinea cruris and tinea manus

6 Correlation of types of lesion with species of fungus has been most successful in cases of tinea pedis and tinea unguium Six types of lesions were noted in each

7 The search for multiple clinical types should be painstaking, since the detection of the type aids not only in ultimate eradication but also in the clinical identification of the etiologic agent

8 Statistics indicate that it is the etiologic agent rather than the type of lesion which influences the possibility of isolation T gypseum is easier to isolate than is T rubrum

Harvard University

1031 South Broadway

SUPERFICIAL MYCOSES OF VETERANS

II Dermatophytosis and Cutaneous Moniliasis, Correlation of Clinical Manifestations and Etiologic Agent

R C BURKE, Ph D
CAMBRIDGE, MASS
AND
F E BUMGARNER, M D
LOS ANGELES

IN THE past few years several efforts have been made to correlate the fungus species with the clinical manifestations of the superficial mycoses Among these studies have been the work of Lewis, Montgomery and Hopper [1] on the clinical manifestations of Trichophyton purpureum and that of Montgomery and Caspar [2] on the clinical manifestations of Tricophyton purpureum, T gypseum and Candida albicans

In a previous paper,[3] we reported on a study of 1,000 veterans with in-service diagnoses of superficial mycoses, 466 of whom had fungous infections as proved by laboratory examination Of these, 416, or 87 1 per cent, showed dermatophytosis, and 13 (3 per cent), moniliasis The 416 patients with dermatophytosis and 13 with cutaneous moniliasis had 819 clinical manifestations of various types of dermatophytosis, falling into the commonly recognized categories of tinea pedis, tinea unguium, tinea cruris, tinea manus and generalized tinea, in that order of incidence

Slides and cultures were made in each case in an attempt to correlate the various types of lesions with the etiologic agents In general this correlation was most successful with tinea pedis and with tinea unguium In tinea manus, in contrast, only slight correlation could be

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1 Lewis, G M , Montgomery, R M, and Hopper, M E Cutaneous Manifestations of Trichophyton Purpureum (Bang), Arch Dermat & Syph **37** 823 (May) 1938

2 Montgomery, R M, and Caspar, E Cutaneous Manifestations of the Fungi Causing Dermatophytosis and Onychomycosis, J A M A **128** 77 (May 12) 1945

3 Bumgarner, F E, and Burke, R C Superficial Mycoses of Veterans I Survey of 1,000 Veterans with Service Diagnosis of Dermatophytosis, Arch Dermat & Syph **60** 742 (Nov) 1949

SARCOMA INVOLVING THE SKIN

ERVIN EPSTEIN, M D
OAKLAND, CALIF

TRADITIONALLY tumors have been divided into those of ectodermal and those of mesodermal origin The malignant neoplasms have been similarly divided into carcinoma, including melanoma, and sarcoma However, this classification is not completely satisfactory, since in some cases epithelioma, especially melanoma, reacts in the body in the same highly malignant manner as sarcoma Furthermore, in some cases sarcoma—in many of the cases neurosarcoma—is actually of ectodermal origin However, common usage makes this classification the most workable at this time

A voluminous literature has developed around the problems presented by cases of cutaneous epithelioma and melanoma While sarcoma is not completely neglected, comparatively little can be found in dermatologic writings concerning it Beerman,[1] in his excellent review on tumors of the skin, did not find enough to enable him to consider sarcoma Yet the dermatologist is often called on to diagnose and eradicate the smaller sarcomatous lesions As will be demonstrated later, sarcoma is among the most difficult to diagnose in the field of cutaneous neoplasms Furthermore, as in the case of epithelioma, cure depends on early recognition of the growth and prompt, adequate therapy

MATERIAL

The statements made in this paper are based on a study of 28 patients with histologically proved sarcoma involving the skin Six of the patients were encountered in private practice The remainder were studied from records made available by cooperating physicians and hospitals [2] In this series all of the neoplasms except 1, diagnosed as rhabdomyosarcoma, are believed to have originated in the skin and its appendages Cases of special types of sarcoma, well recognized by

From the Departments of Dermatology, Highland-Alameda County Hospital, Oakland, and Mount Zion Hospital, San Francisco

1 Beerman, H Tumors of the Skin A Review of the Literature, Am J M Sc **211** 480 (April) 1946, **212** 479 (Oct) 1946

2 This includes Highland-Alameda County Hospital, Mount Zion Hospital, Oakland Veterans Administration Hospital, Drs Norman N Epstein, Herman V Allington, J O Smith, Franklin I Harris, John Sampson and Allan Cohen

made, while in tinea cruris, unfortunately, no dependable correlation could be found The results of study will be discussed for each category, in the following order tinea pedis, tinea unguium, tinea cruris, tinea manus and generalized tinea

TINEA PEDIS

Of the 360 positive cases of tinea pedis, a fungus was isolated in 186, or 51 per cent T gypseum was cultured in 118 cases (63 per cent), Trichophyton rubrum in 58 cases (31 per cent), Epidermophyton floccosum in 4 cases (2 per cent) and C albicans in 6 cases (3 per cent) In other words, T gypseum was encountered about twice as frequently as was T rubrum, and both E floccosum and C albicans were rarely found If only the three dermatophytes are considered, T gypseum was isolated in 64 per cent of the cases, T rubrum in 34 per cent and E floccosum in 2 per cent

The latter figures agree favorably with those of the results obtained by Miss Rhoda Benham, as detailed by Hopkins and associates,[5] who credited her with 111 positive cultures for the periods of 1940 and 1946 The incidence of T gypseum obtained by Benham averaged 64 per cent, that of T rubrum, 25 per cent, and that of E floccosum, 5 per cent Percentages obtained by Lewis and Hopper[6] in 1938 for 153 cultures were not dissimilar T gypseum, 73 per cent, T rubrum, 25 per cent, and E floccosum, 2 per cent

Six types of lesions were identified in cases of tinea pedis chronic intertriginous, chronic hyperkeratotic scaling, chronic papulovesiculosquamous, bullous, subacute and severe chronic hyperkeratotic scaling Table 1 details the total number of cases of each of these types, the percentage in which cultures were obtained and the percentage of each of the etiologic agents

Chronic intertriginous lesions accounted for 41 7 per cent of the 360 clinical cases noted Cultures were obtained from 48 per cent of the cases In this type of lesion it is almost impossible to determine the etiologic agent by clinical examination alone T gypseum was isolated in 54 3 per cent, T rubrum, in 36 per cent, and E floccosum and C albicans, in 1 4 per cent and 8 3 per cent, respectively

Chronic hyperkeratotic scaling lesions of the plantar and medial surfaces ranked second, comprising 19 per cent of the 360 cases Cultures were obtained in only 37 1 per cent of the cases, the majority

4 Footnote deleted on proof

5 Hopkins, J C , Hillegas, A B , Ledin, B L , Rebell, G C, and Camp, E Dermatophytosis at an Army Post, J Invest Dermat 8 291 (June) 1947

6 Lewis, G W , and Hopper, M E An Introduction to Medical Mycology. Chicago, Year Book Publishers, Inc , 1939

TABLE 1.—*Cases of Cutaneous Sarcoma*

o	Sex	Age, Yr	Duration	Race	Location	Metastases	Histology	Prognosis	Treatment
1	M	57	6 mo	W	Shoulder	+	Giant cell sarcoma	Died 3½ yr	Excision, amputation, roentgen irradiation, cyclotron irradiation
2	M	44	6 mo	W	Occiput	0	Fibrosarcoma	Living and well 2 yr	Excision
3	M	23	3 mo	W	Postauricular area	0	Fibrosarcoma	Living and well 7 yr	Excision
4	M	55	9 mo	W	Forehead	0	Fibrosarcoma	?	Excision
5	F	52	1 yr	N	Inguinal region	+	Mixed cell sarcoma	Died 1 yr	Excision, roentgen irradiation
6	M	15	6 mo	W	Scapular	0	Fibrosarcoma	Living and well 3 yr	Excision
7	M	70	4 mo	W	Thigh	+	Giant cell sarcoma	Died 1 yr	Excision
8	F	48	6 yr	W	Thigh	+	Fibrosarcoma	Died 6½ yr	Excision
9	M	46	5 mo	W	Thigh	+	Fibrosarcoma	Died 1 yr	None
10	M	45	4 yr	W	Arms, legs	0	Neurosarcoma (von Recklinghausen's disease) *	Died 10 yr *	None
11	F	26	1 yr	W	Thigh	0	Fibrosarcoma	Living and well 8 yr	Excision
12	M	26	1 yr	N	Shoulder	+	Fibrosarcoma	Died 1½ yr	Excision, roentgen irradiation (12,700r)
13	M	77	?	W	Preauricular area	0	Fibrosarcoma	Died 2 yr *	Excision
14	F	47	1 yr	W	Thigh	+	Rhabdomyosarcoma	Died 2½ yr	Disarticulation
15	F	28	4 yr	W	Popliteal space	+	Fibrosarcoma	Died 4 yr	Excision
16	M	62	2 yr	N	Arm	+	Fibrosarcoma	Died 2 yr	None
17	M	56	15 mo	W	Scapular	0	Fibrosarcoma	Living and well 2 yr	Excision
18	F	49	5 yr	W	Thigh	0	Neurosarcoma	Living and well 6½ yr	Excision
19	F	32	3 mo	W	Abdomen	0	Angiosarcoma	Living and well 9 mo	Excision
20	M	63	20 yr	W	Groin	+	Myxosarcoma	Died 22 yr	Excision, roentgen irradiation
21	M	39	1 yr	W	Foot	+	Fibrosarcoma	Died 2 yr	Excision
22	M	43	19 yr	W	Buttock	+	Fibrosarcoma	Died 20 yr	Excision, roentgen irradiation, phosphorus^{32} irradiation
23	M	67	2 yr	W	Back	+	Fibrosarcoma	Living, with recurrence 7 yr	Excision, roentgen irradiation
24	F	42	3 mo	W	Thigh	0	Fibrosarcoma	Living and well 10 yr	Amputation
25	F	8	2 yr	W	Face	+	Angiosarcoma	Died 3 yr	Excision, roentgen irradiation
26	M	1½	1 yr	W	Axilla	0	Angiosarcoma	?	Radium therapy
27	F	80	1 mo	W	Lip	0	Fibrosarcoma	?	Curettage and desiccation
28	F	37	4 mo	W	Arm, thigh	0	Fibrosarcoma	?	Curettage and desiccation

* The patient died of causes other than sarcoma

(84 6 per cent) of the cultures yielding T rubrum Three of the 4 cases of chronic hyperkeratotic scaling yielding T gypseum occurred in Negroes Several cases of palmar chronic hyperkeratotic scaling due to T gypseum, in both Negro and white patients, were also noted

The chronic papulovesiculosquamous type of lesion occurred in 18 per cent, or almost as frequently as did the chronic hyperkeratotic scaling type It was possible to make cultures from 54 4 per cent of the 68 positive cases Of these cultures, T gypseum was isolated in 75 7 per cent and T rubrum in the others

Bullous lesions ranked fourth (15 per cent) in incidence Cultures were isolated in 74 per cent of the cases, T gypseum being identified in

TABLE 1.—*Type of Lesion and Etiologic Agent in the Cases of Tinea Pedis*

	Chronic Interdigitous Lesions	Bullous Lesions	Chronic Papulovesicular Squamous Lesions	Subacute Lesions	Severe Chronic Hyperkeratotic Scaling Lesions	Chronic Hyperkeratotic Scaling Lesions	Total
Cases	150	54	68	14	4	70	360
Percentage of total	41 7	15	18 9	4 9	1	19 4	100
No cultured	72	40	37	8	3	26	186
Percentage cultured	48	74	54 4	57 1	75	37 1	51
No yielding T gypseum	39	40	28	7		4	118
Percentage yielding T gypseum	54 3	100	75 7	87 5		16 4	63
No yielding T rubrum	26		9	1		22	58
Percentage yielding T rubrum	36		24 3	12 5		84 6	31
No yielding E floccosum	1				3		4
Percentage yielding E floccosum	1 4				100		2
No yielding C albicans	6						6
Percentage yielding C albicans	8 3						3

each instance Combined infection with T rubrum was recorded in 2 instances

Only 14 (5 per cent) subacute lesions (mycosis plus secondary infection) were proved to be tineal Antibacterial treatment was administered to some patients before positive cultures were obtained Cultures were obtained in 57 1 per cent of the cases, T gypseum being identified in 87 5 per cent Subacute lesions were of vesicular or bullous origin

Severe chronic hyperkeratotic scaling was noted in only 4 cases (0 1 per cent), from 3 of which cultures yielded E floccosum It was necessary to reculture material from 2 of these cases before the organism was obtained

One may reason that it is possible to identify the etiologic agent by clinical examination alone in the case of bullous and severe chronic hyperkeratotic scaling lesions—that is, T gypseum in the first instance

dermatologists, as Kaposi's sarcoma and lymphosarcoma, were not included in this study Table 1 presents the 28 cases included in the series

CLINICAL PICTURE

Sarcoma develops in the skin or the subcutaneous tissue as a small nodule If superficially located, it grossly resembles epithelioma Growth may be rapid or slow, although the former is more common The nodule develops to form a mass which becomes elevated, discolored (usually purplish) and later necrotic and ulcerated Bleeding is common Later, the necrotic ulcer becomes fungating and granulomatous Involvement of regional lymph nodes is comparatively infrequent, this having been noted clinically in only 2 cases (7 1 per cent)

Only a single tumor was present in 24 cases (86 per cent) Multiple tumors were found in the other 4 Table 2 gives the location of these tumors There were 61 lesions in the 28 patients The most important finding is that in 39 4 per cent of the cases the lower extremities were

TABLE 2.—*Location of Tumors in this Series*

Location	Cases
Head	6
Trunk	10
Upper extremities	3
Lower extremities	11

involved In 35 8 per cent the trunk was affected Sarcoma was noted on the thighs in 28 6 per cent Epithelioma is definitely unusual in these locations

CLINICAL DIAGNOSIS

Sarcoma is easily diagnosed from its clinical appearance when it has become a massive purplish tumor with necrosis, ulceration and fungating overgrowth However, in no instance in this series was the clinical diagnosis suggested on simple inspection of a small growth The clinical diagnoses in 18 cases in which a tentative diagnosis was offered prior to surgical intervention are given in table 3 In the 3 instances in which the tumor was correctly diagnosed, the lesion was far advanced In the personally observed 6 cases the diagnosis was sarcoma in 1 (a large necrotic mass), squamous cell epithelioma in 1, basal cell epithelioma in 2, granuloma pyogenicum in 1 and fibroma in 1 The only other common diagnosis in the other 22 cases was infectious granuloma, including cutaneous tuberculosis, in 3 cases Therefore, the most important differential problem is that of epithelioma The coincident, adjacent occurrence of epithelioma and sarcoma in 2 cases further complicated the problem of diagnosis

and E floccosum in the second Of the chronic papulovesiculosquamous lesions, T gypseum was the etiologic agent in three fourths and T rubrum in the others Four fifths of the subacute lesions may be assumed to be caused by T gypseum It is not possible to identify by clinical examination alone the fungous species in chronic intertriginous lesions

In addition to the foregoing conclusions, one may infer from the material in table 1 that T rubrum is more difficult to isolate than is T gypseum In the five types of tinea pedis due to species of Trichophyton, the greater the percentage of lesions from which the organism was isolated, the higher the incidence of T gypseum noted For instance, cultures from bullous lesions yielded the etiologic agent in 74 per cent of lesions, T gypseum being isolated in each case, while cultures from chronic hyperkeratotic scaling lesions yielded the agents in only 37 1 per cent of all lesions, T gypseum being noted in 15 4 per cent and T rubrum in 84 6 per cent One may infer that the incidence of T rubrum would be much higher in the case of chronic hyperkeratotic, chronic papulovesiculosquamous and chronic intertriginous scaling, and even subacute lesions, if cultures were obtained from all cases listed

TINEA UNGUIUM

Among the 429 cases of dermatophytosis, there were 245 cases of tinea unguium, of which 222 cases were of infected toe nails and 23 of infected finger nails Infection of the toe nails was noted and proved by laboratory examination in 60 per cent of the cases of tinea pedis Hopkins and associates [5] had observed infected toe nails in 47 per cent of their cases of recurrent tinea pedis

At first, the number of nails involved and the degree of involvement were believed to be of primary importance, but it soon became apparent that there was some correlation between the organism isolated and certain types of involvement of the nail Therefore considerable effort was expended in an attempt to obtain a reliable key which could be used by physicians interested in this problem It is not felt that this key is a complete answer, but it is believed that it forms a basis for future and more exhaustive study

As in cases of tinea pedis, six types of lesions have been noted in cases of tinea unguium, the last two types have been observed only on the hands

Type 1 Leukonychia trichophytica, consisting of white patches on the surface or within the nail plate T gypseum has been reported as the agent always isolated, however, the mycology laboratory isolated T rubrum in 3 out of 5 cases in which cultures were obtained

Table 4 outlines the differential points between sarcoma and epithelioma The most important features may be briefly mentioned Of the cases of sarcoma, 35 8 per cent occur in the precancer age The most common locations for sarcoma are on the extremities and the trunk, areas comparatively infrequently involved by epithelioma The massive growth and necrosis usually make the differentiation obvious Sarcoma is more frequent in Negroes than is epithelioma, and this may be of importance in some cases Sarcoma usually grows more rapidly than epithelioma The lesions of both sarcoma and epithelioma are usually single but may be multiple in either case Sarcoma often develops in

TABLE 3.—*Preoperative Diagnosis in 18 Cases of Sarcoma Involving the Skin*

Diagnosis	Cases	Diagnosis	Cases
Epithelioma	4	Hernia	1
Squamous cell	2	Gout	1
Basal cell	2	Polyarthritis	1
Sarcoma	3	Draining sinus tract	1
"Infectious granuloma"	2	Fibroma	1
Infected wound	1	Granuloma pyogenicum	1
Sebaceous cyst	1	Cutaneous tuberculosis	1

TABLE 4.—*Differential Diagnosis Between Sarcoma and Epithelioma*

Differential Point	Sarcoma	Epithelioma
Age	35 per cent less than 40	Usually over 40
Location	Trunk and lower extremities	Face and dorsa of hands
Clinical picture	Massive overgrowth	Ulceration
Negroes	More frequent	Less frequent
Growth	More rapid	Slower
Onset	Cutaneous or subcutaneous	Cutaneous
Surgical findings (gross)	Necrosis, greater spread than expected	Nodular and ulcerative
Metastases	Common	Comparatively infrequent
Lymph node involvement in presence of metastases	Infrequent	Probably always

the subcutaneous tissue, although it commonly appears in the true skin originally

While simple inspection and palpation may not establish the correct diagnosis, two features are found at surgical intervention that give one invaluable clues to the true nature of the neoplasm Even in small size, sarcoma extends more deeply than one would expect epithelioma of the same apparent size to do and second necrosis is present These features have been of great importance in this series

ETIOLOGY AND INCIDENCE

Obviously, the cause of sarcoma is unknown However, there are certain known factors of interest For instance certain precarcinomatous lesions may also be presarcomatous In this group might be included

TYPE 2 Inverted V infection, with pronounced symmetry, little if any epithelial debris and dulness of the nails (particularly if hyperhidrosis is associated) Usually all the nails on one or both feet are involved T gypseum is isolated in the majority of cases

TYPE 3 Asymmetric infection, with epithelial debris, thickened nail plate, infected nail bed and involvement of from 1 to 10 nails If the nails are in the same stage of involvement and, if the nails, particularly those on the second to fifth digits, are dull, T gypseum is the organism most frequently isolated If the nails are in varying stages of involvement and retain some luster, T rubrum is the fungus most often isolated

TYPE 4 —Ragged, opaque, thick and crumbly nails Both T rubrum (in the majority of the cases) and T gypseum have been isolated from such nails Often various saprophytes are also present In 1 instance, mycelium and conidia of Hormodendrum were noted throughout the nail tissue Several plates were planted with scrapings from the nail, and T gypseum and Hormodendrum sp were both isolated

TYPE 5 Nail uninfected, separated from infected nail bed T gypseum was isolated in 1 case, while in 5 other cases the agent was not obtained This type of lesion was noted only on the hands

TYPE 6 —Transverse ridges in nails which are frequently dull or opaque, with a serous exudate at times and occasional paronychia This is the well known C albicans type of lesion

It was possible to culture the organism from toe nails in 33 per cent and from the finger nails in 56 per cent of the cases The figure given for the toe nails is lower than that obtained in similar studies by Lewis and Hopper, as communicated to one of us (R C B) Final results of the study disclosed that of the 429 patients having dermatophytosis or cutaneous moniliasis, 245, or 57 per cent, had some degree of involvement of the nails All these, with the exception of 18, showed concurrent involvement of the feet or other parts of the body

Kittredge [7] stated that generalized involvement of all the nails was unusual and that the case he reported at the time was the seventh one to be reported Such occurrences, however, are not as unusual as the paucity of literature on the subject would indicate Three such cases, in all of which T rubrum was yielded, were uncovered among the veterans included in this study In addition, 11 cases of tinea unguium of all the toe nails due to T rubrum were recorded In 7 of these 11 cases the patient had acquired the infection in Alabama, Mississippi or Louisiana and presented not only type 3 involvement of all the nails

7 Kittredge, H E Onychomycosis Universalis Trichophytina et Epidermophyta Report of Seventh Case Thus Far Recorded in English, Arch Dermat & Syph **34** 398 (Sept) 1936

lupus vulgaris, xeroderma pigmentosum and radiodermatitis MacKee[3] and others have stated that it is doubtful that sarcoma ever develops in areas of radiodermatitis While cases have been reported in which a lesion developing in such an area histologically resembled sarcoma, he felt that it was actually of epithelial origin In case 2 of this series a lesion diagnosed as sarcoma developed less than 1 inch (2 5 cm) from a lesion diagnosed as squamous cell epithelioma in an area of radiodermatitis The former was of greater duration than the latter, but both lesions were present at the same time and were excised in a single block dissection Histologically there was no resemblance between the two lesions After a study of special stains (Masson's, silver impregnation and phosphotungstic acid) Biskind[4] felt that the sarcomatous lesion was of mesodermal origin[4a] In case 13 three lesions were removed from the face of a 77 year old man at the same time Histopathologic examination revealed that one lesion was basal cell epithelioma, one was mixed cell epithelioma and the third sarcoma

Six apparently unrelated conditions occurred concurrently with sarcoma in this series Four psoriasis, lupus erythematosus, polyarthritis and cholelithiasis—were obviously coincidental, and each occurred in 1 case only Tuberculosis was noted twice Sarcoma was associated with carcinoma in 3 instances This is 10 7 per cent of the entire series but is 16 6 per cent of the patients over 40 years of age, i e , in the cancer age

The evidence presented in the two previous paragraphs causes one to speculate whether the factor that leads to the development of sarcoma is not the same as that which leads to carcinomatous degeneration Apparently there is in certain patients and certain lesions a tendency toward malignant changes, and the malignant cells may be of epidermal or mesodermal origin

Trauma seemed to be important in the development of sarcoma in 5 cases, 17 8 per cent In 4 cases the patient related the onset of the tumor to a severe traumatic incident involving the affected area These included a kick in the buttocks in a fight, a home accident, an automobile accident and an industrial accident In the fifth case, apparently a recurrent low grade sarcoma of twenty years' duration became actively malignant, the growth was accelerated and death occurred two years after an automobile accident The literature is filled with arguments

3 MacKee, G M X-Rays and Radium in the Treatment of Diseases of the Skin, ed 3, Philadelphia, Lea & Febiger, 1938, p 355

4 Biskind, G Personal communication to the author

4a According to a report received from Major Robert B Franklin, Medical Corps, United States Air Force, dated July 29, 1949, this patient was hospitalized because of metastases in the left pleura and the liver Such metastases are much more suggestive of sarcoma than of epithelioma

but also concurrent chronic hyperkeratotic scaling of the plantar surfaces The strains of T rubrum isolated in these cases are being studied because of certain morphologic variations

TINEA CRURIS

Tinea cruris ranked third in prevalence, comprising 86 of the 429 cases of dermatophytosis and cutaneous moniliasis In only 18 of the 86 verified cases was the infection limited to a single site In some of these 18 cases there was a history of possible tinea pedis In 22 cases there were two lesion areas, 18 of which were of the feet and groin In the remaining 46 cases there were three or more lesion sites

Three types of lesions were noted. "eczema marginatum" type, a solid plaque type and the erythematous, exudative monilial type Correlation of the clinical aspects with the etiologic agent has not been possible in the case of tinea cruris Cultures were obtained in only 33 7 per cent (29 cases) of the verified cases Of this number, cultures yielded T gypseum in 8 (27 5 per cent), T rubrum in 16 (55 4 per cent), E floccosum in 1 (3 3 per cent) and C albicans in 4 (13 8 per cent) This small number does not provide sufficiently valid percentages, but comparison of the figures for T gypseum and T rubrum (omitting those for C albicans) indicates that, where the true dermatophytes are concerned, T rubrum is the etiologic agent in about 66 per cent of the cases of tinea cruris

TINEA MANUS

Tinea manus ranked fourth in incidence of the clinical types of dermatophytosis In all, 254 cases of service-diagnosed "ringworm of the hands" were studied Only 48 cases were established definitely as of tinea manus The majority of the cases in which this disease was not established were characterized by vesicular and exudative lesions, located particularly on the fingers

In only 10 of the positive cases were the hands alone involved, in 9 cases the feet and hands were involved, and the remaining 27 yielded three or more positive lesion sites There was a definite racial distinction observed in that only 5 Negroes (a ratio of 1 Negro to 3 white patients) were shown to have tinea manus T gypseum was recovered from lesions on the hands of 2 Negroes and T rubrum from another

With regard to origin of infection of the hand and wrist, an interesting factor was noted One third of the patients with verified lesions had a history of having worked with motor fuels and machinery at the time of onset

regarding the importance or the lack of importance of trauma in initiating malignant changes Five more cases will not settle these arguments

There were 17 men and 11 women in this series However, in other reported studies there does not seem to be any significant difference in sex incidence

Twenty-five of the patients were white, the other 3 were Negroes Apparently, the Negro does not possess immunity from sarcoma paralleling his comparative freedom from certain other types of cancer, including basal cell epithelioma Furthermore, all 3 Negroes died of their sarcoma in an average of eighteen months The longest survival in a Negro in this group was two years This is a much shorter period of survival than the average for the entire series (5 35 years)

The age at the time of onset is given in table 5 This demonstrates that no age group is exempt The youngest patient was 1½ years of age, the oldest, 80 years of age Thirty-five and seven-tenths per cent of the patients were less than 40 years old the so-called precancer age

TABLE 5—*Age at Onset of Sarcoma*

Years	Cases	Years	Cases
0 to 10	2	41 to 50	8
11 to 20	1	51 to 60	4
21 to 30	4	61 to 70	4
31 to 40	8	71 to 80	2

The 6 personally observed cases were culled from about 9,000 dermatologic cases, an incidence of 1 in 1,500 However, this incidence seems high, as I do not recall seeing sarcoma in any other group of dermatologic patients that have been under my care According to Eller,[5] primary sarcoma of the skin accounts for only 5 to 6 per cent of cases of all types of sarcoma occurring in the human body

PATHOLOGY

It is not the purpose of this paper to reiterate the well established criteria for the histologic diagnosis of sarcoma However it should be realized that despite clearcut textbook descriptions it is often difficult to establish the diagnosis of sarcoma For instance, MacKee,[3] as previously stated, claimed that the lesions arising in areas of radiodermatitis that have been diagnosed as sarcoma by general pathologists are in reality spindle cell epithelioma Montgomery [6] stated that most so-called

5 Eller, J J Tumors of the Skin Benign and Malignant, 1939, Lea & Febiger, Philadelphia, p 434

6 Montgomery, H Epithelomas of the Arm Simulating Endothelioma Sarcoma and Sporotrichosis Two Unusual Cases, M Clin North America **19** 605 (Sept) 1935

Three definite and distinct types of lesions were observed in tinea manus a chronic hyperkeratotic scaling, most frequently involving the palms and ventral surfaces of the fingers, a chronic papulovesiculosquamous eruption, which may involve the palm but which most frequently manifests itself on the dorsum of the hand and on the wrist, and a bullous type involving the palmar areas

The chronic hyperkeratotic scaling type has been observed most frequently, it was seen in 34 (65 4 per cent) of the total of 52 cases of different types of lesions Scaling is variable but usually fine and branny It was expected that T rubrum would always be isolated from this type, particularly since that was the general rule with chronic hyperkeratotic lesions of the feet However, of the 19 cases in which cultures were obtained only 14 (73 7 per cent) yielded T rubrum, the cultures in the other 5 (2 Negroes and 3 white patients) having yielded T gypseum (table 2)

TABLE 2—*Type of Lesion and Etiologic Agent in Cases of Tinea Manus*

	Chronic Hyperkeratotic Scaling Lesions	Chronic Papulovesiculosquamous Lesions	Bullous Lesions	Not Listed	Total
Cases	34	12	1	5	52*
Percentage of total	65 4	23 8	1 9	9 6	100
Number cultured	19	9	1	5	32
Percentage cultured	55 9	75 0	100	60 0	61 5
Trichophyton gypseum	5	4	1	1	11
Percentage of T gypseum	26 3	44 4	100	33 3	34 3
Trichophyton rubrum	14	5	0	2	21
Percentage of T rubrum	73 7	55 5	0	66 6	65 7

* Four cases with both chronic hyperkeratotic scaling and chronic papulovesicular squamous lesions were observed

Chronic papulovesicular squamous lesions of the dorsum of the hand and wrist were observed in 12 cases In 9 of these, cultures were obtained In 4 the organism was identified as T gypseum and in 5 as T rubrum Several patients with this type of lesion of the hands had generalized dermatophytosis as well The bullous type of tinea manus was observed only once, on the thenar and hypothenar eminences of the left hand of a 26 year old Negro He also had bullous lesions of the feet T gypseum was identified from cultures of both areas

Of the 32 cultures made in cases of tinea manus, in 21, or 65 7 per cent, T rubrum was identified We believe that the greater part of the 44 per cent of uncultured chronic hyperkeratotic scaling lesions and of the 25 per cent of uncultured chronic papulovesicular squamous lesions were probably due to T rubrum This belief rests, in part, on evidence presented in table 1 and table 2, which indicates that T gypseum is

cases of sarcoma of the extremities are actually cases of epithelioma Furthermore, it is often difficult to determine whether a lesion is a sarcoma or very cellular, nonencapsulated benign fibroma This is well illustrated by the case reported by Eller and Kest [7] Biopsy specimens were sent to a number of leading skin and tumor pathologists The following diagnoses were offered by these admitted experts D L Satenstein and D Wilbert Sachs—"small spindle cell sarcoma with hemorrhage", Emmerich von Ham "fibrosarcoma", Hamilton Montgomery—"angiosarcoma", Paul Klemperer—"fibrosarcoma", J Frank Fraser—"fibrosarcoma", Fred D Weidman "fibrosarcoma", Francis Carter Wood—"neurofibroma" In a study of cases presented before various dermatologic societies in this country it is obvious that this is not an unusual experience

This demonstrates the difficulty of accepting histologic observations as the only proof of the diagnosis of sarcoma It is a medical axiom that the laboratory results must be correlated with the clinical findings in all

TABLE 6—*Histologic Types of Sarcoma*

Type	Cases
Fibrosarcoma	18
Angiosarcoma	3
Giant cell sarcoma	2
Neurosarcoma	2
Mixed cell sarcoma	1
Rhabdomyosarcoma	1
Myxosarcoma	1

branches of medicine Therefore, it is suggested that the diagnosis of sarcoma must be based not only on the histopathologic aspects but on the clinical findings and on the course of the neoplasm as well

In this series the diagnoses were made by 12 different pathologists While any given histopathologic section was examined by more than one pathologist in only a few instances, the fact that so many pathologists were involved ruled out the possibility that this series was influenced unduly by personal factors on the part of the examiner Furthermore, the mortality of 54 2 per cent speaks eloquently for the obvious fact that, whatever criteria are employed, most of these cases were instances of highly malignant sarcoma

The histologic types of the tumors are given in table 6 The cases of giant cell sarcoma may be included in the group of cases of fibrosarcoma, so that the latter diagnosis was made in 71 5 per cent of the total number of cases of sarcoma of the skin In other words, fibrosarcoma occurred three times as frequently in the skin as did all the other forms of sarcoma

7 Eller, J J, and Kest, L H Sarcoma Arising in an Organized Hematoma Resulting from a Single Trauma, Arch Dermat & Syph **43** 813 (May) 1941

easier to isolate than is T rubrum Additional evidence rests on correlation of types of lesions with etiologic agents In other words, if a patient presents a chronic hyperkeratotic lesion of the feet from which T rubrum has been isolated and a chronic hyperkeratotic lesion of the hand not yielding a culture, one may expect with a high degree of certainty that T rubrum is also the etiologic agent of the tinea manus

TABLE 3.—*Dermatophytosis and Cutaneous Monilasis*

	Number of Patients	Total Number of Patients	Percentage
Patients with single sites of infection		183	42 6
Feet	130		
Toe nails	18		
Groin	18		
Hand	10		
Finger nails	1		
Buttocks	4		
Leg	1		
Trunk	1		
Patients with two sites of infection		179	41 7
Feet, nails	140		
Feet, groin	18		
Feet, hands	9		
Feet, finger nails	2		
Groin, finger nails	2		
Gro'n, perineum	1		
Groin, toe nails	1		
Toe nails, finger nails	6		
Patients with three sites of infection		33	7 7
Feet, nails, groin	18		
Feet, na ls, hand	7		
Feet, nails, finger nails	1		
Feet, hand, leg	1		
Feet, groin, perineum	1		
Feet, groin, upper trunk	1		
Hand, groin, neck	1		
Nails, groin, buttocks	3		
Patients with four sites of infection		21	5 0
Feet, nails, hand, finger nails	6		
Feet, nails, groin, axilla	2		
Feet, nails, groin, hand	2		
Feet, nails, hand, leg	4		
Feet, nails, leg, groin	1		
Feet, nails, abdomen, groin	1		
Feet, nails, groin, buttocks	4		
Groin, leg, arm, axilla	1		
Patients with generalized infection		13	3 0
Total		429	100

GENERALIZED DERMATOPHYTOSIS

Table 3 lists patients with verified dermatophytoses according to sites For 42 6 per cent (183 patients) there was evidence of one positive site, for 41 7 per cent (179 patients) of two positive sites, for 7 7 per cent (33 patients), of three positive sites, for 5 per cent (21 patients) of four positive sites, and in 3 per cent (13 patients), of five or more positive sites For the last-mentioned patients the infection was termed generalized 10 of the 13 patients were white, and 3 were

combined This is in contrast to the statements of Stewart and Copeland [8] and of Cutler, Buschke and Cantril,[9] who expressed the belief that soft tissue sarcoma is in most cases neurosarcoma In only 2 cases of this series was there evidence of associated von Recklinghausen's disease or of a tumor of a nerve trunk or of an unusual amount of nerve tissue in the sarcoma

Autopsies were performed in 9 cases Metastatic lesions were demonstrated in all 9 and, furthermore, the cell type of the metastases was identical with that found in the primary cutaneous tumor Death was due to cachexia or to terminal incidents, such as bronchopneumonia or nephritis The locations of the metastatic lesions are listed in table 7 This table indicates that metastases occurred most frequently in the lungs and the pleura, followed by the bones, the skin, the lymph nodes and the liver Autopsies revealed involvement of the deep lymph nodes more often than one would expect on clinical examination, suggesting that dissemination may occur through the lymphatic channels as well as through the blood stream

TABLE 7 —*Locations of Metastases Observed in 9 Autopsies*

Location	Cases	Location	Cases
Lungs and pleura	8	Heart	1
Skin	4	Kidney	1
Lymph nodes	4	Spleen	1
Bones	4	Peritoneum	1
Endocrine glands (adrenals, pancreas, pituitary)	3	Omentum	1
		Gallbladder	1
Liver	3	Subcutaneous tissue	1

PROGNOSIS AND TREATMENT

Obviously, therapy is imperative in this highly malignant condition In 13 of 24 cases in which there was a follow-up period of nine months or more, the patient had already died of metastases at the time of the last observation This is a mortality rate of 54 2 per cent Undoubtedly, this percentage would increase with more prolonged observation Two patients died of other causes, and their deaths are not included as resulting from sarcoma In these 13 cases the average period from the onset of symptoms to death was 5 4 years In the 11 cases in which the patient is still living or has died from other causes the average survival is 5 3 years The total for the entire group was 5 35 years

8 Stewart, F W, and Copeland, M M Neurogenic Sarcoma, Am J Cancer **15** 1235 (July) 1931

9 Cutler, M , Buschke, F, and Cantril, S T Cancer Its Diagnosis and Treatment, Philadelphia W B Saunders Company, 1938, pp 659-666

Negroes Since white persons constituted two thirds of the total number studied, incidence by ratio was about the same for white persons as for Negroes

Cultures were isolated from 10 of the patients T rubrum was obtained from 8 white patients and T gypseum from 1 Negro and 1 white person Since T rubrum is more difficult to isolate than is T gypseum, one may assume that T rubrum is the cause of more than 80 per cent of the cases of generalized dermatophytosis

The most extensive case observed by us was that of R T, a 28 year old machinist, who stated that he had incurred the infection four years previously while he had been in the Navy The condition had remained chronic since that time and had gradually spread to cover three fourths of the body Both hands and feet showed chronic hyperkeratotic scaling of the palmer and plantar surfaces All toe nails and finger nails were infected Lesions of the chronic papulovesiculosquamous type extended from the area of the groin over the abdomen and buttocks and down the inner aspects of the thighs almost to the knees Similar lesions covered the forearms, the shoulders, the upper portion of the trunk and the neck and even extended onto the scalp T rubrum was isolated from several areas

TABLE 4.—*Sites of Generalized Tineal Infections*

Total Number of Patients	13
Total Number of Sites	95
Average Number of Sites per Patient	7.3

Site	Number of Patients	Site	Number of Patients
Feet	12	Finger nails	5
Groin	11	Abdomen	4
Buttocks	9	Scalp	4
Hands	9	Axilla	4
Toe nails	8	Concha of ear	4
Upper part of trunk	8	Arm	3
Legs	7	Face	1
Neck	6		

SUMMARY

1 Of the various clinical types of dermatophytosis, tinea pedis ranked first in incidence, followed in order by tinea unguium, tinea cruris, tinea manus and generalized tinea

2 Multiple clinical types of dermatophytosis were noted in more than half the patients with verified infections

3 Chronic hyperkeratotic scaling is recognized as being the most frequent type of tinea manus, occurring in about 66 per cent of the verified cases

4 Infected toe nails occurred in 60 per cent of the cases of tinea pedis In only 18 of the 245 cases of tinea unguium was there no clinical or laboratory evidence of concurrent dermatophytosis

The longest life was twenty-two years, and the shortest in the fatal cases was one year after the appearance of the primary tumor

The earlier treatment is instituted, the better the prognosis If one employs a duration of six months as an arbitrary dividing line between early and delayed treatment, one finds that the mortality in the early-treated group was 30 per cent of the 10 patients receiving prompt attention On the other hand the mortality in 14 receiving treatment more than six months after the onset was 71 4 per cent While the number of cases studied may not be significant, these figures support the obvious thesis that the earlier adequate treatment is instituted, the better the prognosis It is to the credit of both the patients and the physicians that almost 35 per cent of the patients received treatment less than six months after the appearance of the tumor

Three patients were untreated throughout the course of their sarcoma All died, the average period of survival being 4 3 years However, this

TABLE 8.—*Mortality with Each Type of Treatment*

Type of Treatment	Patients	Mortality
Excision	21	9 (42 7%)
Roentgen irradiation	7	6 (85 8%)
Amputation	3	2 (66 6%)
Curettage and electrodesiccation	2	0
Cyclotron irradiation	1	1 (100%)
Phosphorus ^{32} irradiation	1	1 (100%)
Radium irradiation	1	0
None	3	3 (100%)

comparatively favorable average is unduly influenced by the inclusion of a patient with a questionable diagnosis of low grade neurosarcoma This patient died ten years after the onset of his sarcoma, but death was due to an intercurrent tumor of the bladder diagnosed as carcinoma The average for the other 2 patients was 1 5 years, a figure which is probably closer to the true outlook for patients with untreated cutaneous sarcoma

It is difficult to compare different schemes of treatment because the prognosis depends on many factors, such as duration of the lesion prior to the onset of treatment, race, thoroughness of treatment and presence or absence of metastases Furthermore, a small series does not allow dogmatic statements Many patients received more than one form of treatment Table 8 shows the number of patients receiving each type of treatment and the number dying despite the approach utilized

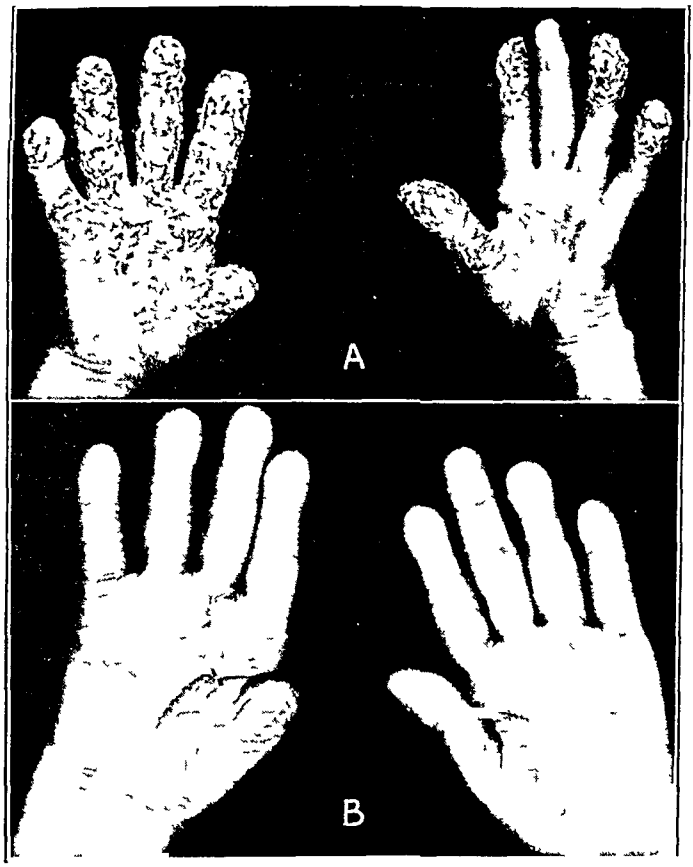
It is important to note that more than 50 per cent of the patients treated by excision, with or without auxiliary measures, were still living at the time this study was conducted Furthermore, of 13 patients treated with excision alone, 7, or 53 8 per cent, survived Of 6 patients whom I personally treated by radical cautery excision, 4 are living and

Kaposi's Sarcoma Presented by DR JAMES H MITCHELL, DR RALPH SCULL and (by invitation) DR B YAFFE

Hidrosadenitis Suppurativa, Acne Vulgaris and Acne Conglobata, DR E E SENFAR and staff

Pustular Psoriasis, Healed After Tobacco Juice Soaks Presented by DR STEPHEN ROTHMAN and (by invitation) DR J H MCCREARY

S J, a housewife aged 57, was presented at the Chicago Dermatological Society meeting of Oct 16, 1946 The diagnoses suggested were pustular



Pustular psoriasis treated with tobacco juice soaks *A,* before treatment *B,* after treatment

psoriasis and acrodermatitis continua She had been hospitalized at the Albert Merritt Billings Hospital from June 12 to October 22 for observation and treatment

The patient was discharged from the hospital, unimproved, one week after the presentation, to be followed as an outpatient While at home, on her own initiative, she soaked her hands in hot tobacco juice six to eight times a day The juice was prepared by boiling tobacco in water for two minutes Each soaking lasted five to ten minutes Within one week considerable improvement

was seen in all the treated lesions, and almost complete cure of the hands and fingers was achieved in four weeks

Dr Edward Laden of our department could not demonstrate any antibiotic effect of the tobacco juice in vitro

Dermatitis Repens, Therapeutic Result Presented by DR F E SENEAR and staff

E L, aged 63, has been a patient on the dermatology service, Illinois Research and Education Hospital, since October 1946, with the diagnosis of dermatitis repens, affecting the first and second toes of the right foot On a previous admission intractable pain associated with a similar eruption on the left foot had necessitated amputation up to the middle of the thigh During the present period of hospitalization the following therapeutic agents were tried without noticeable improvement penicillin parenterally in large doses, sulfonamide drugs, staphylococcic toxoid, wet dressings of silver nitrate potassium permanganate and benzalkonium chloride, tyrothricin dressings, streptomycin ointment and repeated lumbar sympathetic blocks The most recent treatment has included a course of sulfapyridine by mouth and roentgen irradiation (twelve doses of 50 r, given twice weekly, terminating on May 12, 1947) No improvement was noted Immediately after application of compound tincture of benzoin ointment was started (May 28), oozing and crusting disappeared and epithelization began At present there is only a small area of dry healing granulations at the tip of the great toe

Pustular Psoriasis, Treated with Tobacco Juice Soaks Presented by DR STEPHEN ROTHMAN and (by invitation) DR J C MCCREARY

M K, a white housewife aged 53, was admitted to Albert Merritt Billings Hospital May 18, 1947, presenting widespread psoriasis of forty-eight years' duration Approximately fifteen years ago the palm of the right hand became pruritic and then pustular Some of the joints of the hand stiffened Later the tips of the fingers and toes became red, swollen and full of pustules Some nails were shed Repeated cultures failed to grow bacteria There have been remissions with improvement, of several years' duration, but never complete healing The present flare-up began four months prior to admission

In the past, various methods of therapy had been tried, including local applications of tyrothricin, penicillin, nitrofurazone, chloresium, ammoniated mercury, tar, roentgen irradiations, systemic administration of arsenic and vitamin B complex and a fat-free diet

Examination revealed well circumscribed, erythematous, partly crusted and partly hyperkeratotic patches on the scalp, trunk and upper and lower extremities The hands and toes showed subcorneal pustulation and crusting The right hand showed atrophy and contractures Both hands had stiffened interphalangeal joints Some finger nails and toe nails were missing, others were rudimentary

Wassermann and Kahn reactions of the blood were negative The urine was normal Examination of the blood revealed 12,800 leukocytes The differential count was normal Hemoglobin was 12 8 Gm Erythrocyte cells numbered 3,370,000 Blood lipids and cholesterol were normal The results of the sternal bone marrow examination was normal The basal metabolic rate was + 2 per cent A roentgenogram of the hands showed moderate arthritic changes involving the interphalangeal joints The electrocardiogram showed a tendency to left axis deviation

well without evidence of recurrence or metastases after an average survival period of 2 75 years One patient succumbed to metastases three years postoperatively There was no opportunity to make follow-up studies on the sixth patient [10]

Amputation does not offer a better prognosis than simple excision, provided, of course, that the latter is adequately performed In addition, excision avoids the permanent disability that follows amputation For instance, patient 11 presented a large nodular fibrosarcoma of the thigh of one year's duration The histologic section was classified as grade 2 The lesion was completely excised, and the patient is living and well eight years later Of perhaps even greater importance, she has been able to lead a normal life, having had two successful pregnancies since and being able to raise her children

Irradiation may cause regression of the tumor, but there is no evidence that it is curative Most authorities agree that these types of sarcoma are radioresistant Radiation therapy should not be used as a substitute for surgical removal nor can postoperative radiation act as a safety mechanism to compensate for inadequate excision

SUMMARY

A study of 28 patients with histologically proved sarcoma involving the skin is presented

The lesions start as small nodules, which become massive, necrotic, ulcerated, fungating tumors

Epithelioma is the most important of the lesions to be differentiated from sarcoma and the most difficult to differentiate

Precarcinomatous lesions may be presarcomatous, and patients with sarcoma may have associated carcinoma

To diagnose sarcoma on purely histologic grounds is difficult and may be fallacious The histologic observations should be correlated with the clinical findings and course

The earlier treatment is instituted, the better the prognosis The mortality was almost 250 per cent greater in the group receiving treatment after six months than in those being cared for less than six months from the onset of the tumor

Adequate excision is apparently the treatment of choice

447 Twenty-Ninth Street

10 These statistics must be modified, as metastastic lesions developed in 1 other patient while this paper was in press See footnote 4a

ment is most applicable to the matured "polar" lesions, it is least true with reference to the macular lesions It will be instructive, however, and of great practical value, for one to try to apply this observation to the simple, flat, usually hypopigmented macular lesions of the disease

Bacterioscopy The bacillary content of the tissue fluid at the border of the lesion is perhaps the most useful criterion If material obtained by Wade's "scraped incision" method [3] (which is still inaccurately but concisely called a "snip" in Hawaii) shows abundant bacilli, the lesion is probably lepromatous, if it shows few or none, the lesion is probably tuberculoid, if it shows moderate numbers, the nature of the lesion has not yet been determined, and the case, though not classifiable as either lepromatous or tuberculoid in type, may be said to be in the indeterminate group, at least so far as bacterioscopic evidence is concerned

The examination for bacilli may also be made on sections of tissue, preferably with the aid of Fite's formaldehyde modification [4] of the Ziehl-Neelsen stain More sensitive methods of searching for bacilli (as described by de Souza-Araujo [5]) are useful in diagnosis but not particularly helpful in differentiating the types

Neurologic Findings Concomitant and coextensive nerve damage is probably of almost equal importance in classifying the case as tuberculoid Demonstrable anesthesia which is identical in extent with the hypopigmentation is strong evidence that the lesion is not lepromatous but maculoanesthetic, i e, tuberculoid in immunologic type if not (yet) in histologic structure, for it is in this type that the neurolytic defensive reaction to the bacillus occurs In this connection, it is often forgotten even by experienced workers that anesthesia in leprosy is apt to occur in a dissociated pattern, e g, anesthesia to cold or heat or to both, with unimpaired sensitivity to light touch and to pinprick, is commonly found in early lesions In lesions manifesting no apparent anesthesia, the histamine test of Rodriguez and Plantilla [6] may be employed (in patients with light-colored skins) to detect lesser degrees of nerve dam-

3 Wade, H W Bacteriological Examination in Leprosy, Leprosy Rev 6 54 (April) 1935

4 Fite, G L The Staining of Acid-Fast Bacilli in Paraffin Sections, Am J Path **14** 491 (July) 1938, The Fuchsin-Formaldehyde Method of Staining Acid-Fast Bacilli in Paraffin Sections, J Lab & Clin Med **25** 743 (April) 1940 Tilden, I L, and Tanaka, M Fite's Fuchsin-Formaldehyde Method for Acid-Fast Bacilli Applied to Frozen Sections, Am J Clin Path **15** 95 (Nov) 1945

5 de Souza-Araujo, H C Clamp Method to Obtain Cutaneous Lymph in the Diagnosis of Leprosy, Leprosy Rev **18** 44 (April-July) 1947

6 Rodriguez, J, and Plantilla, F C The Histamine Test as an Aid in the Diagnosis of Early Leprosy, Philippine J Sc **46**·123 (Sept) 1931 Internat J Leprosy **1** 49 (Jan) 1933

BERYLLIUM GRANULOMAS OF THE SKIN

FRANK R DUTRA, M D
CINCINNATI

IN A RECENT paper, Grier, Nash and Freiman [1] have reviewed the literature relating to the effects which beryllium may have on the skin and subcutaneous tissues They recognized four distinct types of cutaneous reaction to beryllium Contact dermatitis occurs in persons working with soluble salts of beryllium, particularly beryllium fluoride or beryllium sulfate [2] Ulcers result when crystals of soluble beryllium salts become embedded in the tissues, these heal only after the crystals have been removed surgically or have been extruded spontaneously [2] In some patients suffering from chronic pulmonary berylliosis, granulomas of the skin occur, and these are similar to the granulomas which develop in the lungs [3] Grier and his co-workers have observed a fourth variety of cutaneous reaction to beryllium which they term "subcutaneous granuloma occurring in persons who cut themselves on fluorescent lamps"

Tissues received from 4 persons in whom subcutaneous granulomas developed after beryllium compounds had been traumatically introduced into the skin have been examined at the Kettering Laboratory We have also received tissues from an additional person in whom granulomatous inflammation of the subcutaneous tissues followed the introduction of metallic beryllium

CLINICAL DATA

The clinical data were essentially similar for all 5 patients In 4 the beryllium was embedded in the skin as the result of the accidental breaking of fluorescent lamp tubes and the puncturing of the skin by

This work was done under a contract with the Office of Naval Research

From the Kettering Laboratory of Applied Physiology, University of Cincinnati, College of Medicine

1 Grier, R S , Nash, P , and Freiman, D G Skin Lesions in Persons Exposed to Beryllium Compounds, J Indust Hyg & Toxicol **30** 228-237, 1948

2 Van Ordstrand, H S , Hughes, R , De Nardi, J M , and Carmody, M G Beryllium Poisoning, J A M A **129** 1084-1090 (Dec 15) 1945

3 Hardy, H L , and Tabershaw, I R Delayed Chemical Pneumonitis Occurring in Workers Exposed to Beryllium Compounds, J Indust Hyg & Toxicol **28** 197-211, 1946 Pyre, J , and Oatway, W H , Jr Beryllium Granulomatosis, Alias Miliary Sarcoid, Salem Sarcoid, Miliary Sarcoidosis, Chronic Beryllium Poisoning, or Delayed Chemical Pneumonitis, Arizona Med **4** 21-29, 1947

age, in darker skins the sweating tests described by Muir [7] and Degotte [8] (using intradermally administered pilocarpine or exercise) or by Myerson [9] and his associates (using methacholine), which seem to be just as sensitive may be used to better advantage [10] The important thing is the demonstration of nerve damage which is coextensive with the visible macule, this is highly characteristic of the maculoanesthetic—the "neural" or tuberculoid—form of leprosy

Clinical Aspects The remaining clinical features by which one may judge the hypothetic macule constitute much less useful criteria of its type The classic lepromatous macule tends to be multiple, and the tuberculoid, solitary, but many exceptions occur The lepromatous macule generally has a poorly defined border, often with fine pseudopod-like irregularities, the tuberculoid macule is usually sharply outlined By the same token, lepromatous macules tend to confluence and tuberculoid ones to discreteness Lepromatous macules are likely to occur on the trunk, a macule on the face or extremities is more commonly of the tuberculoid variety The lepromatous macule usually persists for many months or alternatively progresses into the clinical lesion known as a leproma, the anesthetic macule is likely to show evidence of regression within six months to a year None of these findings, however, is conclusive, and if the bacterioscopic and neurologic criteria are inconsistent one must resort to biopsy Indeed, biopsy should be done anyway, as a routine precaution

Histologic Changes Histologic changes in such early and minimally advanced lesions as the macules being discussed are pretty likely to be banal so far as the general pathologist's interpretation of them is concerned Ermakova, of Moscow,[11] found them so in a considerable series of anesthetic flat "macules" Wade,[12] on the other hand, found changes which he regarded as "nearly always in some degree tubercu-

7 Rogers, L, and Muir, E Leprosy, ed 3, Baltimore, Williams & Wilkins Company, 1946

8 Degotte, J Practical Application of Sweating Dysfunction to the Diagnosis of Leprosy, Rec tr sc med Congo, January 1942, p 135

9 Myerson, A, Loman, J, and Rinkel, M Human Autonomic Pharmacology VI General and Local Sweating Produced by Acetyl-Beta-Methyl Choline Chloride (Mecholyl), Am J M Sc **194** 75 (July) 1937 Arnold, H L, Jr The Sweat Response to Intradermally Injected Mecholyl Preliminary Report of Its Possible Use in the Diagnosis of Leprosy, Proc Staff Meet Clin, Honolulu **11** 75 (Aug) 1945

10 Arnold, H L, Jr The Intradermal Mecholyl Test for Anidrosis, A Diagnostic Aid in Leprosy, Internat J Leprosy **16** 335 (July-Sept) 1948

11 Ermakova, N The Histopathology of Simple Leprids, Internat J Leprosy **7** 495 (Oct-Dec) 1939

12 Wade, H W, and Rodriguez, J N The Skin Lesions of Early Leprosy II Observations in Cebu, Internat J Leprosy **5** 1 (Jan-March) 1937

fragments of glass The fluorescent powder which lines tubes of this type is comprised of a calcined mixture of zinc oxide, manganese oxide, beryllium oxide and silica In these 4 patients the lacerations healed with production of excess fibrous tissue Two of the lesions, when first seen by physicians, were believed to be simple keloids All four lesions, on one or more occasions after initial healing, opened to discharge thick,

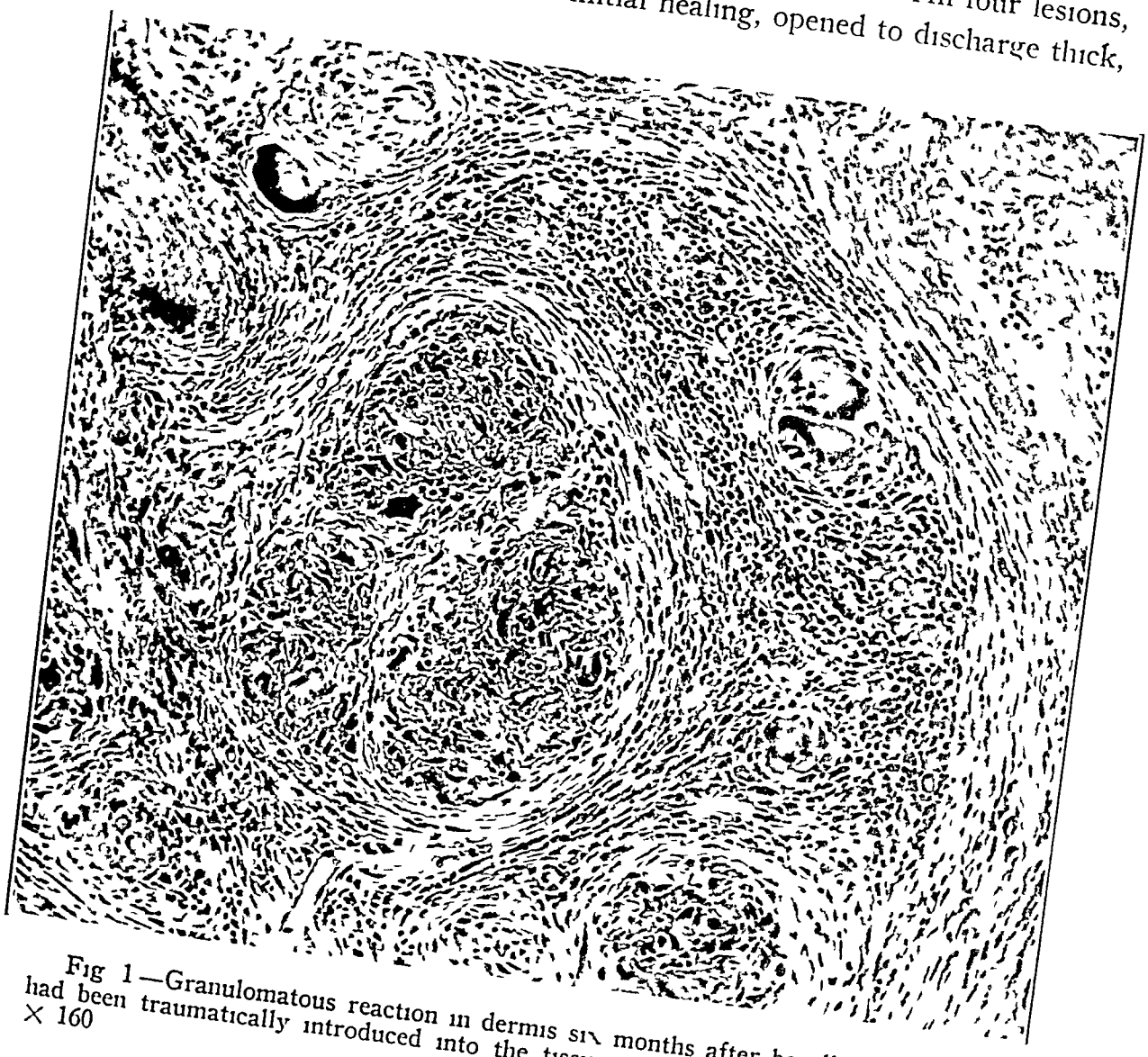


Fig 1—Granulomatous reaction in dermis six months after beryllium phosphor had been traumatically introduced into the tissues, hematoxylin and eosin stain, × 160

grayish white necrotic material The period from injury to excision varied from four months to nine years

A fifth patient discussed here was a young woman who worked at cutting metallic beryllium with a machine and had accidentally lacerated her finger during her work A granuloma developed, and this failed to heal over a period of four years, so that finally a complete excision of the lesion was made

loid" in a larger series of similar lesions He often found it necessary to employ serial sections, however Ota and Sato,[13] in Japan, came independently to exactly the same conclusion in the same year

What is meant by "in some degree tuberculoid"? Not fully developed, noncaseating, epithelioid cell tubercles, to be sure In general, the designation refers to an infiltrate of rather sharply focal arrangement, composed of both lymphocytes and epithelioid cells, which may or may not be arranged in the pattern of definite tubercles Diffuseness or vague margination of the infiltrate and scarcity of lymphocytes are both suggestive of the lepromatous form of the disease

THE INDETERMINATE GROUP

If bacterioscopic, neurologic, clinical and histologic changes are inconclusive or inconsistent, the problem is a more difficult one, it may indeed be incapable of solution for the time being The South American dermatologists, perhaps impatient at the postponement of an exact diagnosis, have urged the establishment of a third "type" or "form" of leprosy to include all such cases they suggested calling them *incaracterístico* (uncharacteristic) At the Fifth International Congress for Leprosy, in April 1948, the words "indeterminate" and "group" were agreed on the former because it permitted the use of the same initial letter, *I*, in Portuguese, Spanish, French and English, and the latter to indicate that this term designated, not a third type of leprosy, but only a group of cases, defined largely by their lack of definitive characteristics It has been shown that such cases may remain in this neutral status for a variable period, at the end of which they will heal, become lepromatous or become tuberculoid

In addition to the differentiating criteria which have been discussed, there is one more point, regarded by some workers as the most informative and important of all, which presents so many ramifications that I shall discuss it under a separate heading

LEPROMIN (FERNÁNDEZ AND MITSUDA) REACTIONS

Kensuke Mitsuda reported in 1916[14] that the intracutaneous injection of a small amount of a phenolized, boiled suspension of finely divided lepromatous granulation tissue (a mixture of dead Mycobacterium leprae and human tissue) would produce a slowly developing often ulcerated papule in the great majority of patients with the "maculoanesthetic" (i e, tuberculoid) form of leprosy, as well as in many

13 Ota, M, and Sato, S Tuberculoid Changes in Leprosy Internat J Leprosy 5:199 (April-June) 1937

14 (*a*) Mitsuda, K, in discussion in Jap J Dermat **16**:513 (June) 1916, (*b*) cited by Hayashi, F Mitsuda's Skin Reaction in Leprosy, Internat J Leprosy **1** 31 (Jan) 1933

HISTOPATHOLOGIC OBSERVATIONS

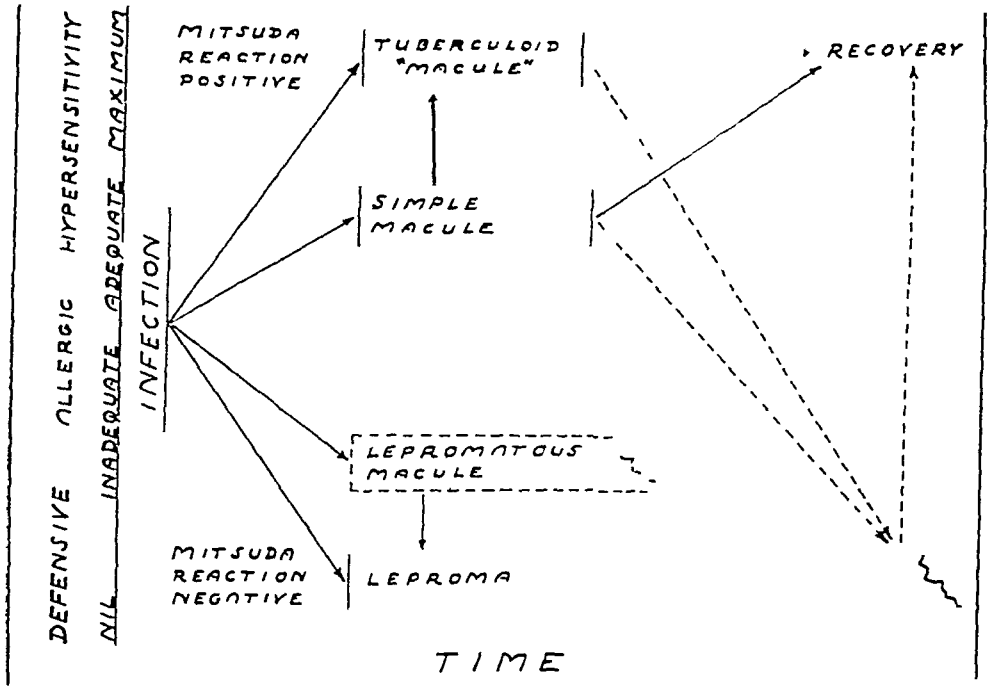
The tissues which were excised four months after the phosphor-containing beryllium oxide had been introduced into them were found to be the site of a granulomatous reaction in which there were areas of



Fig 2.—Focal necrosis and granulomatous inflammation of dermis four years after metallic beryllium had been introduced into the tissues, hematoxylin and eosin stain, × 160

necrosis The necrotic areas involved the dermis and subcutaneous tissues, and they were not unlike the areas of caseation in tuberculosis, they were, however, much more extensive than those in the rare cases

presumably uninfected persons, it regularly produced little or no reaction in the great majority of patients with the "tubercular" (the nodular, or lepromatous) form He extended and amplified his observations in a series of reports, which received little attention in this country until the publication of a paper by his student, Hayashi, in 1933 [15] His observations have since been widely confirmed Numerous studies have been made in an effort to improve and standardize the test by purification and fractionation of the test material These have not been especially rewarding, however, since the crude preparation seems as potent as and no less specific than, its various fractions [16]



Diagrammatic oversimplification of the major cutaneous lesions of leprosy as functions of (1) "defensive allergic hypersensitivity" to the bacillus and (2) time Note that this hypersensitivity may already exist at the time of infection, that it may either increase or decrease after infection occurs, that it may be demonstrated by a positive Mitsuda reaction, that it results, in general, in self limited lesions known as "macules," that its failure to develop results in essentially persistent or progressive lesions and that it rarely, if ever, develops late in the course of the disease Note, too, that exceptionally this hypersensitivity may be lost, resulting in transition of the disease to the lepromatous form and that, also exceptionally, recovery will occur in a lepromatous case, without, however (or sometimes with?), transition through a tuberculoid phase

The term "defensive allergic hypersensitivity" is to be taken loosely, not literally And the prognosis as indicated does not take into account the effect of treatment with sulfone derivatives

15 Hayashi [14b]

16 Davey, T F Some Observations on the Role of Allergy in Leprosy, Leprosy Rev **17** 42 (July), 75 (Oct) 1946

of Boeck's sarcoid in which caseous necrosis does occur [4] There was amorphous, slightly eosinophilic, granular material, and at one point a small, highly refractile mass of foreign material was present Around the necrotic center there were large mononuclear cells, some of which were polyhedral while others were spindle-shaped These cells had large reticular nuclei, so that they resembled epithelioid cells The necrotic areas were surrounded by a zone of partially degenerated, elongated cells resembling fibroblasts, around which there was cellular

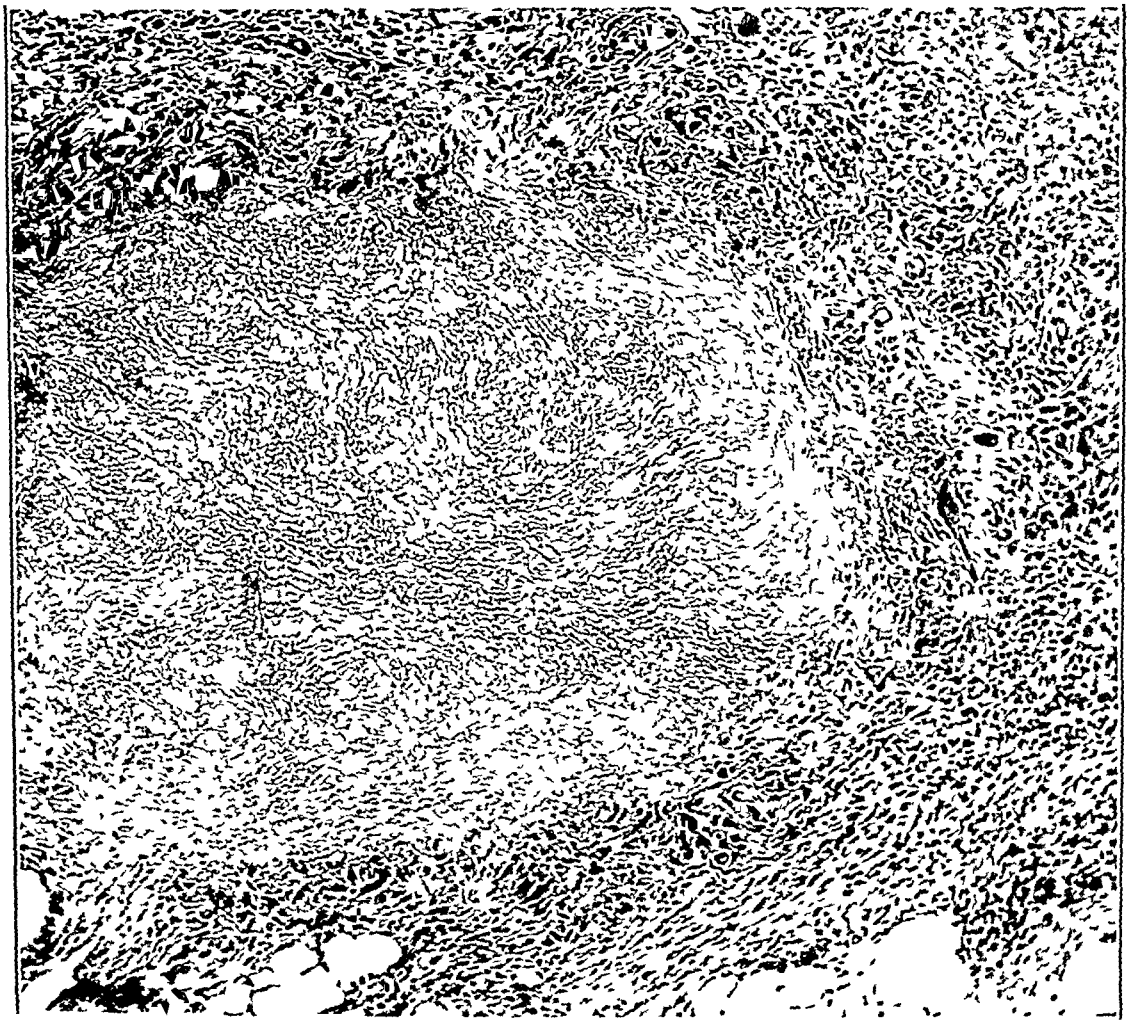


Fig 3—Area of necrosis of dermis four months after introduction of beryllium phosphor, hematoxylin and eosin stain, × 115

collagenous tissue infiltrated with large numbers of lymphocytes The remainder of the tissue was divided by relatively dense strands of connective tissue into nodules of varying sizes The nodules were comprised in most instances of relatively loosely arranged connective tissue, in which there were elongated and polygonal cells with large reticular nuclei, surrounded by elongated fibroblasts and a few lymphocytes The

4 Goldman, L Personal communication to the author

Fernandez,[17] in 1940, reported that the often observed tuberculin type of reaction to lepromin, reaching peak severity in forty-eight hours instead of the two to five weeks required for the Mitsuda reaction, could be correlated with the clinical form of the leprosy virtually as closely as could the latter Dharmendra and Lowe,[18] in 1943, showed that this response could be elicited regularly by injection of the purified protein, presumably the nucleoprotein, of the bacilli The injection of the crude antigen, on the other hand, generally produced relatively little effect until the bacilli had had time to break down and liberate this antigenic material It is highly probable, at all events, on the basis of this evidence and the analogy with some (though by no means all) forms of tuberculosis, that a positive lepromin test indicates acquired allergic hypersensitivity to the antigens of the leprosy bacillus, though this may have been acquired without infection by, or even contact with, the organism in question I know of no student of leprosy who believes that a strongly positive Mitsuda reaction can occur in a patient with low resistance to leprosy, or a negative or even a feeble reaction in one with high resistance The allergic response and the defensive one seem, in leprosy, inseparable

Hayashi[14b] and others showed that the Mitsuda reaction may be more pronounced in tuberculoid "macules" than in normal skin This observation was confirmed most recently by Davey[16] The reaction is apt to be stronger in elevated tuberculoid "macules" than in flat ones and is usually strongest in their borders A positive reaction is also occasionally found, according to Davey, in lepromatous macules, even when the normal skin outside the macule gives a negative reaction Dharmendra,[19] in a recent extensive review of the literature on the lepromin test, stated that he had not been able to confirm this observation, and my experience in Hawaii has been similar

SIMPLE (FLAT) MACULES VERSUS TUBERCULOID (ELEVATED) "MACULES"

I have discussed in some detail the features of the two types of flat macules, the lepromatous and the anesthetic, or simple The elevated or tuberculoid, "macules" present no such highly refined problem in differentiation, for in them the allergic hypersensitivity to Myco leprae is strongly and usually securely established The histologic changes which are almost invariably of the tuberculoid pattern, with

17 Fernandez, J M M The Early Reaction Induced by Lepromin, Internat J Leprosy 8 1 (Jan-March) 1940

18 Dharmendra and Lowe, J Studies of the Lepromin Test, Leprosy in India **15**.82 (April) 1943, Leprosy Rev **17** 9 (April) 1946

19 Dharmendra The Lepromin Test A Review, Leprosy Rev **18**.92 (Oct) 1947

entire nodules were surrounded by relatively dense connective tissue in circumferential arrangement In the centers of some of the nodules and in the peripheral portions of others were multinucleated giant cells of the Langhans type, some of which were as small as 20 microns in diameter, while others were as much as 200 microns in diameter Some of these giant cells had within their cytoplasm small masses of highly refractile substance, but in none were there inclusion bodies of the type described by Schaumann [5] or of the type described by Wolbach [6]

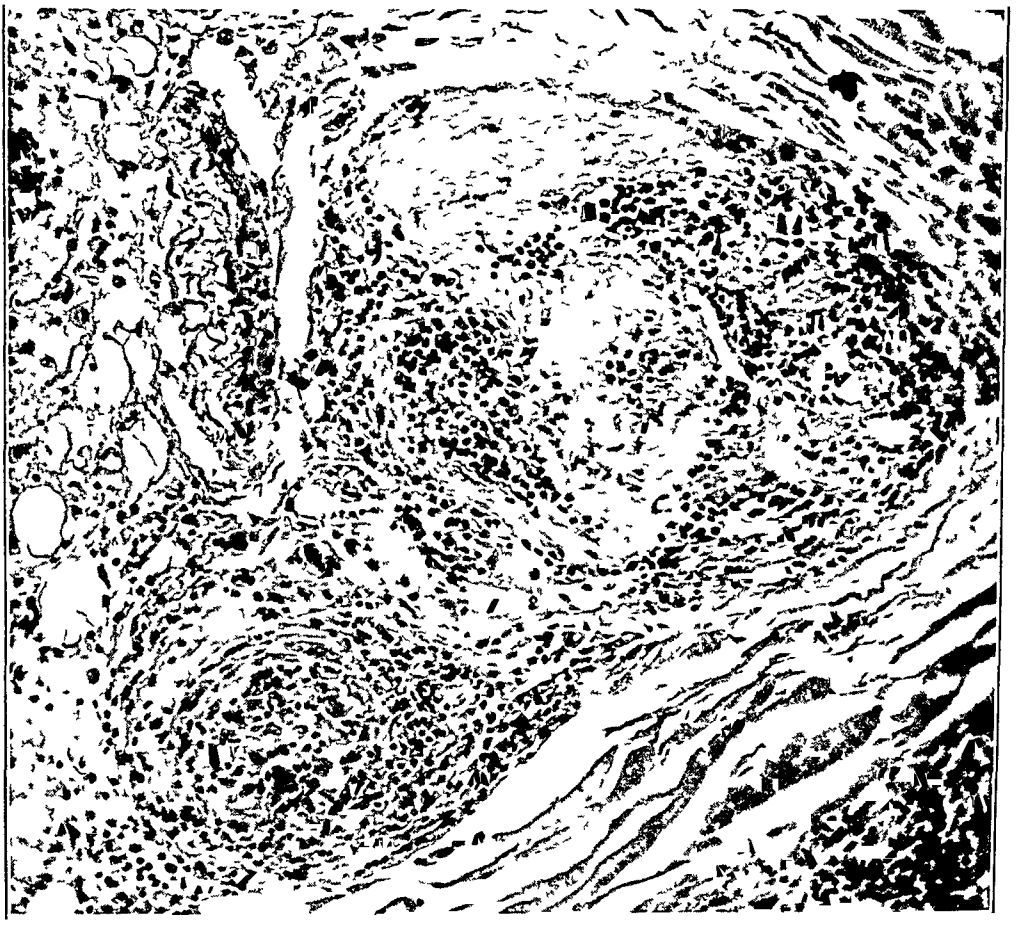


Fig 4—Marked fibrosis of individual nodules in granuloma nine years after beryllium phosphor was introduced into dermis, hematoxylin and eosin stain, × 160

The lesions occupied the dermis and the uppermost portion of the subcutaneous tissues The epidermis was intact, and there were

5 Schaumann, J On the Nature of Certain Peculiar Corpuscles Present in the Tissue of Lymphogranulomatosis Benigna, Acta med Scandinav **106** 239-253, 1941

6 Wolbach, S B A New Type of Cell Inclusion, not Parasitic, Associated with Disseminated Granulomatous Lesions, J M Research **24** 243-257, 1911

well defined, noncaseating, epithelioid cell tubercles and no or comparatively few bacilli; bear out this statement, in accordance with the observations of Jadassohn and Lewandowsky It seems probable that in these lesions there is elaboration of abundant antibody by the histiocytes in the skin, and a resultant antigen-antibody reaction which effectively eliminates the bacilli Why this inflammatory reaction is rarely accompanied with necrosis when it occurs in the skin, and is usually accompanied with it when it occurs in the nerves, is not clear, but this finding has often been reported,[20] and my observations in Hawaii have regularly confirmed it Of course this necrosis of nerve tissue is the reason for the regular occurrence of anesthesia or anhidrosis in even the earliest "macules," and it has led to the confusion begun by Danielssen and Boeck [21] (and checked only for a time by Hansen and Looft [2]), resulting from the designation "anesthetic" or "nerve" or "neural" for cases of this form of the disease and also for lepromatous cases with more nerve damage than cutaneous damage

It may be significant that there is not necessarily any difference between this tuberculoid response, produced by presumably living Myco leprae, and a positive Mitsuda reaction, produced by dead ones, for, indeed, as Davey [16] pointed out, if the former happens to be vigorous and intense enough, or to be accompanied by sufficiently pronounced fixation of the bacilli in the tissues, it may run the same swift and benign course as the Mitsuda test, with final complete resolution in a few weeks or months Ordinarily, however, the multiplication of bacilli, ahead of (or in) the advancing border of the lesion, is able to keep slightly ahead of the development of the defensive tissue reaction, so that gradual spread occurs, and only after some months, or even longer, does either the "anchoring" of the bacilli or the more effective production of antibodies permit all the organisms to be destroyed, so that the lesion heals Healing often occurs in the central zone and spreads peripherally, so that annular lesions from a few millimeters to several decimeters in diameter are formed, and "cockade" patterns, produced by successive fluctuations in the vigor of the antigen-antibody reaction, are not unusual Such patterns are not infrequently observed in patients whose disease is undergoing transition from the tuberculoid to the lepromatous type

The effectiveness and persistence of this combined defensiveness and hypersensitivity may vary widely Transitory relapses after complete or partial healing of the lesions are not rare Even gradual, persistent

20 Ota and Sato [13] Pardo-Castello, V , Tiant, F R , and Piñeyro, R Nerve Lesions of Leprosy, Arch Dermat & Syph **55** 783 (June) 1947

21 Danielssen, D C, and Boeck, C W Traite de la spedalskhed ou elephantiasis des grecs, Paris, J -B Baillière, 1848

moderate acanthosis, hyperkeratosis and parakeratosis The peripheral portions of the lesions were infiltrated by numerous lymphocytes, but within the lesion itself such cells were relatively few

The lesions from 3 other patients who had had phosphors embedded in their skin for periods of from one to four years before excision were similar to the one described The lesion from the woman who had had metallic beryllium embedded in her skin for a period of four years was also similar to the one described

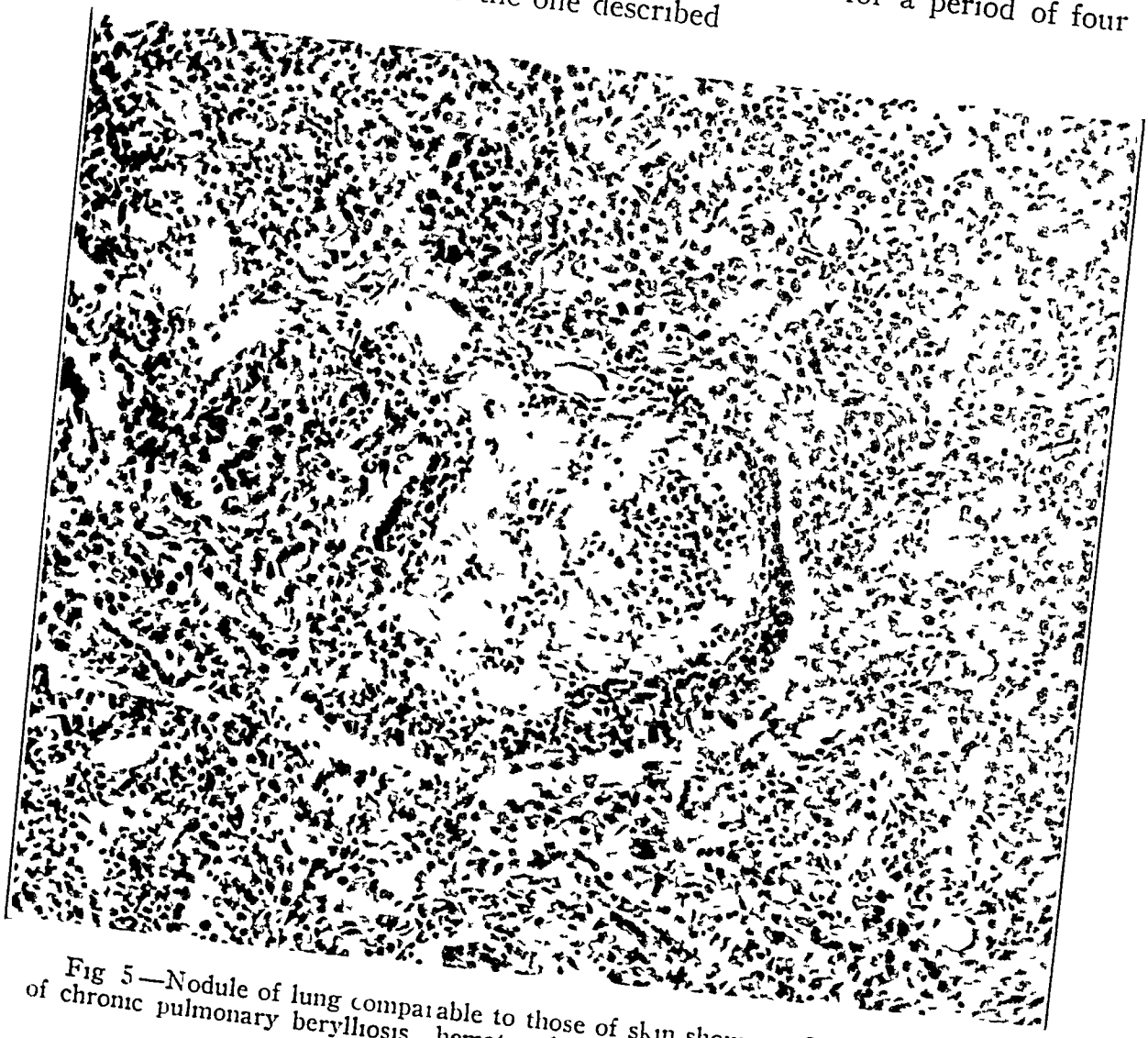


Fig 5—Nodule of lung comparable to those of skin shown in figure 4, in a case of chronic pulmonary berylliosis, hematoxylin and eosin stain, × 160

The lesion in the skin of the man who had had beryllium phosphor embedded at that site nine years before it was excised differed somewhat in degree of development from those the duration of which had been four years or less In the nine year lesion the general picture was one of dense, relatively acellular collagen in which were numerous small nodules comprised of large cells The latter were for the most part compactly arranged, with poorly defined pale cytoplasm and large vesicular nuclei Occasional small multinucleated cells which resembled

loss of hypersensitivity, with resultant reversal of the lepromin reaction to negative and transformation of the lesions from tuberculoid to lepromatous, may occur, though it is so infrequent that some workers have never observed it and some, indeed, doubt that it occurs I have seen it occur twice, both times in patients with large and numerous "major tuberculoid" lesions The first alarming sign was the tendency of both patients to have frequent exacerbations of the cutaneous lesions (tuberculoid reactions) Wade [22] described this process in detail in a few cases The reverse of this phenomenon of transition (i e, a change from the lepromatous to the tuberculoid type) seems to be much rarer, presumably because the patient will usually develop hypersensitivity and resistance to the bacillus early in the course of his infection if he is capable of developing them at all The only definite evidence that transformation in this direction can occur, in fact, was presented recently by Lauro de Souza Lima [23]

TUBERCULOID "MACULES" VERSUS LEPROMAS

In considering tuberculoid "macules" in contrast with lepromas, one is dealing with the easily distinguished "polar" lesions of the disease the two extremes, one representing victory for the patient's defensive processes and the other representing victory for Myco leprae All that was said about the differentiation of the lepromatous macule from the simple or anesthetic macule may be applied here The tuberculoid "macule" (whether macule or plaque) is regularly anesthetic, the leproma is anesthetic only if (as occasionally happens) it occurs in an anesthetic area of skin The tuberculoid "macule" typically contains few or no bacilli, even in reactions, it rarely contains the abundance of bacilli found regularly in a leproma The tuberculoid "macule" characteristically shows noncaseating, epithelioid cell tubercles, with abundant lymphocytes, histologically, the leproma has the architecture and composition of a fatty foreign body granuloma, or xanthoma, in which the lipid material is presumably furnished by the masses of Myco leprae, and in which lymphocytes are few

Clinical features, as with the flat macules, are less trustworthy, however, like flat tuberculoid macules, tuberculoid plaques are somewhat more likely to be solitary, or few, and asymmetric, and lepromas, generalized and symmetrically distributed Lepromas tend to develop earliest and most conspicuously on acral parts ears, forehead chin, buttocks, elbows and fingers Tuberculoid lesions show little or no

22 Wade, H W, and Rodriguez, J N Borderline Tuberculoid Leprosy, Internat J Leprosy 8:307 (July-Sept) 1940

23 Lima, L de S, and de Souza Campos, N Immuno-Biologic Anomalies in Leprosy Internat J Leprosy 16:9 (Jan-March) 1948

Langhans' cells were present There was a large number of lymphocytes scattered throughout these nodules, interspersed between the large cells Many of the nodules had dense collections of numerous lymphocytes in their peripheral portions, and practically all of the nodules were surrounded by collagen which contained only a few small connective tissue cells In some places this collagen was hyalinized

In 3 of the 5 cases sufficient amounts of tissue were available to permit chemical analysis The tissues were analyzed for beryllium by the method of Cholak and Hubbard,[7] and small quantities of beryllium were recovered in 2 cases but could not be recovered in the third

COMMENT

The evidence which supports the opinion that beryllium is capable of producing fibrosis has been presented in a paper[8] in which 13 cases of chronic pulmonary berylliosis with fibrosis and granulomas are described Among 7 cases of acute pneumonitis due to the inhalation of fumes or dusts containing beryllium, there were organization of exudate and early fibrosis in 5, and the lesion progressed to the first stage of the formation of fibrous nodules in 3 Further support of the opinion that beryllium is capable of inducing fibrosis has come from experimental work in which the reactions induced by metals embedded in bone were studied[9] It was found that a certain alloy containing nickel, cobalt, chromium and molybdenum was innocuous, but that when beryllium was added to the alloy in the concentration of 1 6 per cent, granulation tissue formed at the site of the alloy and lymphocytes infiltrated the tissues

The diagnosis of beryllium granuloma of the skin can probably be made clinically when there is a history of beryllium or one of its compounds having been embedded in the skin Lacerations produced by glass from fluorescent lamp tubes are likely to lead to the development of beryllium granulomas, since beryllium oxide is a constituent of the phosphorescent powders used in making these tubes Tissues into which the material has been introduced will, over some months, show formation of excessive scar tissue, which occasionally opens and drains Biopsy of such tissues reveals lesions which could be confused with caseous tuberculosis or Boeck's sarcoid Differentiation rests on the presence of beryllium demonstrated by analytic methods, and on the absence of

7 Cholak, J, and Hubbard, D M Spectrographic Determination of Beryllium in Biological Material and in Air, Analyt Chem **20** 73-76, 1948

8 Dutra, F R The Pneumonitis and Granulomatosis Peculiar to Beryllium Workers, Am J Path **24** 1137-1166, 1948

9 Campbell, E H , Meirowsky, A , and Tompkins, V Studies on the Use of Metals in Surgery II Experiments in the Use of Ticonium in Cranial Repair, Ann Surg **116** 763-775, 1942

real predilection for these parts A sharply defined and elevated border or a clearing center is much more likely to be manifested in a tuberculoid lesion than in a leproma, though the sharply clear center, with a less clearly defined outer margin, suggests the leproma rather than the tuberculoid lesion Norman Sloan [24] pointed out that lepromas have a strong tendency to respect facial and other natural grooves and creases, such as the nasolabial fold and the angle between the root of the nose and the inner corners of the eyes, a tuberculoid plaque will often invade and involve such areas Involvement of the mucous membrane (of the eye, mouth, nose, throat and larynx) and testicular involvement occur only in lepromatous cases Nerve involvement occurs regularly in both lepromatous and tuberculoid cases, but nerve damage is produced only slowly by the gentle, passive, bacteriophagic lepromatous response, whereas it is produced early and rapidly by the vigorous, defensive, bacteriolytic tuberculoid response

SUMMARY AND CONCLUSIONS

The flat macules and elevated "macules" of leprosy apparently represent circumscribed cutaneous areas of acquired allergic hypersensitivity to the nucleoprotein of Myco leprae

If this hypersensitivity is lacking or inadequate to destroy the organisms, the macule is called a lepromatous macule, and it can usually be identified as such by the abundance of bacilli in it and its failure to manifest anesthesia or other evidence of nerve damage

If this hypersensitivity is adequate to destroy the organisms, the lesion is then often spoken of simply as a "macule" (or, better, a tuberculoid plaque), and it can usually be recognized by its relative lack of bacilli and the regular occurrence of evidence of nerve damage throughout its visible extent If such lesions are flat they are sometimes called "simple macules" or "anesthetic macules", if they are elevated they are usually called "tuberculoid macules" Both terms were included under Unna's word "leprides"

The development of an adequate degree of resistance and allergic hypersensitivity to Myco leprae results in the establishment of a relatively favorable form of leprosy which has been known as the "anesthetic" (Danielssen, 1847), "maculoanesthetic" (Hansen, 1895), "neural" and, more recently, "tuberculoid" form

The failure of development of such a state following infection with Myco leprae results in the establishment of an unfavorable form of leprosy known as the "tubercular" (Danielssen), "nodular" (Hansen), "cutaneous" and, more recently, "lepromatous" form

24 Sloan N R Personal communication to the author

tubercle bacilli The beryllium lesion can be differentiated from Boeck's sarcoid by the presence of caseous areas and by the large number of lymphocytes scattered throughout, particularly in the periphery of the lesion It is probable that tertiary syphilis might simulate the cutaneous beryllium granuloma, and the differentiation would depend on the demonstration of treponemas and the failure to demonstrate beryllium Nodular leprosy and certain cutaneous fungous diseases would present only minor difficulties of differentiation

The treatment of cutaneous and subcutaneous granulomas which follow the introduction of beryllium or its compounds has been successful in the 5 cases reported here only when the tissues containing the foreign material have been completely excised Before excision, in each case, the lesion was marked by excessive formation of scar tissue and repeated episodes of discharge of the wound, followed by temporary healing

SUMMARY

Five cases of chronic granulomatous inflammation of the skin and subcutaneous tissues following the introduction of beryllium or beryllium compounds are presented

The histologic relationship of the granulomas of the skin and similar granulomas which occur in the lungs of persons who have inhaled beryllium-containing dusts in industry is described

Cure followed excision of the lesions in all cases

Such hypersensitivity, once developed, usually results in eventual spontaneous cure of the infection, it may, however, be lost, with resultant transition of the case from the tuberculoid to the lepromatous category

The lepromin test appears to be a fairly trustworthy method of measuring this hypersensitivity, both in normal skin and in macules

The Clinic, South Hotel Street at Thomas Square (13)

ABSTRACT OF DISCUSSION

DR BRAULIO SÁENZ, Habana, Cuba The last time our Association met on the Pacific coast was in 1938, at Del Monte, Calif At that meeting I presented a paper on tuberculoid leprosy (ARCH DERMAT & SYPH **39** 456 [March] 1939), the first on this subject in North America The paper was written prior to the holding in Cairo of the Fourth International Congress for Leprosy and was read shortly thereafter It was at that congress that the South American classification of leprosy was rejected and the Cairo classification adopted

My paper, being a pioneer one and based on a limited number of observations, was no doubt incomplete and not devoid of some minor erroneous interpretations Ten years later, on April 10, 1948, the Fifth International Congress for Leprosy took place in Habana, and the South American classification (now known as the classification of Habana) was adopted Dr Arnold has very aptly outlined his paper on this classification, which, for the time being, is the only one tenable, because it is based on the following points (1) the morphology, or clinical aspect of the lesions, (2) immunologic reactions, (3) bacteriologic criteria and (4) a more or less definite histopathologic picture

The presenter stresses the importance of these fundamental bases and discusses the position of the indeterminate groups, previously called uncharacteristic This, as he indicates, may be the possible weak point of this classification, but one must remember that, not only in leprosy, but also in many other dermatologic processes, only the evolution determines the real position of certain cases and that borderline cases are often observed In addition, this group, in the majority of cases, presents a negative reaction to the Mitsuda test, which is a possible indication of future transition to the lepromatous form

The publications of F Fischl (*Dermat Ztschr* **55** 274 [March] 1929), and of Jadassohn (ARCH DERMAT & SYPH **21** 355 [March] 1930) and the communications of I Darier, Civatte, P Woringer and H Gougerot to the International Dermatological Congress at Budapest in 1935 (Deliberationes Dermatologorum Internationalis, IX-1, Budapest, September 1935, Leipzig, Johann Ambrosius Barth, 1936) made important contributions explaining the role of the biologic reactions of immunity on the morphologic aspects of the cutaneous lesions, nevertheless, some points remain unanswered For example, some have denied the possibility of the transformation of the tuberculoid lesions to the lepromatous form, despite such denial, this transformation is an established fact Dr Arnold has observed 3 such cases, and I have seen 4 Some three months ago, I requested Dr Nelson Souza Campos who has had considerable experience in the treatment of patients in the Sanatorio Padre Bento São Paulo, Brazil, for his opinion on the subject He replied to the effect that he had observed 64 cases of tuberculoid leprosy of the reactional type which had undergone transformation to the lepromatous type All cases were observed in patients in leprosy asylums The possible explanation is that these patients had been superinfected from other lepromatous patients This explanation did not apply to my patients who were all encountered in my private

"MACULES" OF LEPROSY

HARRY L ARNOLD Jr, M D
HONOLULU, HAWAII

THE WORD "macule" has long been used by students of leprosy in two quite different and yet overlapping senses Exceptionally, it has been used in the orthodox sense of a circumscribed, flat discoloration of the skin (usually hypopigmentation, and less often erythema), and in this use it is, oddly enough, usually qualified as either "lepromatous" or "simple" (or "anesthetic") or, more recently, "uncharacteristic" or "indeterminate"

The term has been much more commonly used, however, in a sense at once looser and more restricted, and certainly not at all orthodox Without any qualifying adjective, the word "macule"[1] has been used to designate any circumscribed, discolored (hypopigmented erythematous or both) cutaneous lesion, flat or elevated, in which (1) evidence of nerve damage (usually anesthesia) can be demonstrated and (2) bacilli are rare or absent When such a lesion is flat, it is often spoken of as a simple or an anesthetic macule, when it is elevated (and sometimes even when it is not), it is often called a tuberculoid 'macule"

There is, then, a morphologic macule, which is (by definition) flat but may occur in either the lepromatous or the tuberculoid form of leprosy, and an immunologic "macule," which may be either a (flat) macule or an elevated plaque but occurs only in the tuberculoid form of leprosy The lepromatous macule, for reasons which will be discussed presently, occurs relatively infrequently This fact has led to the practice of using the unqualified word "macule" almost entirely as a designation for the circumscribed, anesthetic, paucibacillary macules and plaques—the leprides of Unna which characterize the maculoanesthetic or "neural" or, as the Fifth International Congress for Leprosy named it, the tuberculoid form of the disease

LEPROMATOUS MACULES VERSUS "MACULES"

As Hansen observed over fifty years ago,[2] the "two forms [of leprosy] are clinically pretty sharply distinguishable" This state-

From the Clinic
Read at the Sixty-Eighth Annual Meeting of the American Dermatological Association, Inc, San Diego, Calif, April 26, 1948

1 Quotation marks will be used throughout this article wherever the word is being used in this sense rather than in the literal dermatologic sense

2 Hansen, G A, and Looft, C Leprosy in Its Clinical and Pathological Aspects translated by N Walker, Bristol, J Wright & Co, 1895

practice Therefore, I should like to ask Dr Arnold whether his cases were encountered in an asylum or in private practice Through the action of the sulfone drugs, the reverse of this transformation was reported to the Fifth International Congress for Leprosy by Lauro de Souza Lima (*Internat J Leprosy* **16** 127 [April-June] 1948) Lepromatous leprosy was transformed into the tuberculoid type The histopathologic changes from one form to the other were checked at different dates, the tissular changes appearing first as the expression of an acquired immunity, later the reaction to the Mitsuda test became positive, and as a final stage came the curability of some of the cases Before closing I wish to congratulate Dr Arnold heartily on his timely paper, it is simple and concise, and it gives complete descriptions of the polar and of the indeterminate forms of leprosy, as well as valuable information to the dermatologist respecting correct diagnosis, prognosis and epidemiology of the disease

I also wish to express my satisfaction for the opportunity I have been given to open the discussion on this excellent contribution, in addition, it gives me pleasure to inform Dr Arnold that I have been requested to advise him that he has been proposed as a correspondent member of Sociedad Cubana de Dermatologia y Sifilografia, and of Academia Espanola de Dermatologia y Sifilografia, as a reward for his qualifications as a dermatoleprologist

DR LOUIS WINER, Los Angeles I wish to compliment Dr Arnold on his excellent paper My associates and I have had such cases on two occasions in Los Angeles These cases histologically were definitely tuberculoid in structure On use of the Ziehl-Neelsen stain, numerous acid-fast bacilli were observed The reaction to the lepromin test was negative Because of these observations we were unable to classify the patients However, the indeterminate group provides a classification modification, so that now these patients can be classified I think that the histologic characteristics of tuberculoid formation are indicative that a better prognosis can be expected than if these characteristics were not present

DR HAMILTON MONTGOMERY, Rochester, Minn I should like to ask Dr Arnold and Dr Saenz about recent reports in the literature regarding the reaction to lepromin in patients with sarcoid and tuberculosis It would appear that in sarcoidosis there is a negative reaction, whereas in active pulmonary tuberculosis the reaction may be positive If such observations are substantiated, the lepromin test might be of diagnostic value in northern climates where leprosy is not endemic in distinguishing between an annular sarcoid and a tuberculoid leprosy Both show an epithelioid tuberculoid reaction histologically, so that in older literature in Scandinavian countries the question was raised as to whether the patient had sarcoid or tuberculoid leprosy Tuberculoid leprosy, I understand, gives a positive lepromin or Mitsuda reaction

DR FRED D WEIDMAN, Philadelphia I should like to ask Dr Arnold whether he is able to get a supply of *Nachtblau,* which Dr Pardo-Castello told us about and which is superior to the ordinary Ziehl-Neelsen technic for staining the bacilli

I have tried to secure a supply, without success Does he think that the Fite technic is also superior?

DR HARRY L ARNOLD JR, Honolulu, Hawaii I am obliged to all the discussers Dr Saenz asked whether the transitional cases were private or asylum cases they were all asylum cases, 1 in Mexico and 2 in Hawaii, and all showed typically tuberculoid annules with the "cockade" pattern, with numerous bacilli and (in those seen in Hawaii, at least) a negative reaction to the lepromin test Dr Winer's cases with tuberculoid lesions with numerous bacilli may be examples of

Biopsy of left knee joint capsule showed no abnormalities Biopsy of the skin showed changes typical of pustular psoriasis

While the patient was in the hospital, fever therapy was employed four times, with typhoid vaccine given intravenously (each reading 102 F) with no effect On June 4 the patient started soaking one finger in hot tobacco juice Within three days the swelling had gone and the finger had so improved that the patient was encouraged to soak the right hand Treatment has been continued in the following manner The tobacco is boiled for two minutes in water The hands are soaked in the heated extract for thirty minutes, four to six times a day The solution should be as warm as the patient can tolerate without burning

DISCUSSION

DR S W BECKER I think that the disease in all these patients is of the acrodermatitis continue type rather than the pustular psoriasis type The woman with the lesion on the arm shows a definite atrophy following healing, which rules out psoriasis The results from the bizarre treatment are certainly remarkable

DR F E SENEAR We have had this subject up here so often that nearly everything is repetitious I would like to agree with Dr Becker that the disease in these cases, at least the cases of extensive disease, is of the acrodermatitis continue type rather than pustular psoriasis I think that anyone would point out these lesions on the forearm as being a point against acrodermatitis continue, but the lesions on the tips of the fingers with the extensive undermining of the periphery are suggestive of the Hallopeau type

DR ROBERT M B MACKENNA, London, England (by invitation) I agree with everything Dr Senear has said Most of my colleagues would regard these as acrodermatitis continue type of lesions and not pustular dermatitis

DR STEPHEN ROTHMAN The patient started this treatment on her own She heard about it from neighbors The tobacco is boiled for two minutes only Our main purpose in showing these patients was to ask the members of this society to send more patients to us for testing the efficacy of this method with fractions of the tobacco juice in order to isolate the active compounds Of course, we shall need a number of patients with pustular psoriasis and with acrodermatitis Hallopeau to carry out this work

Lupus Vulgaris Improved with Vitamin D_2 Presented by DR F E SENEAR and staff

Lupus Miliaris Disseminata Facei, Improvement from Treatment with Vitamin D_2 Presented by DR HAROLD SHELLOW

Fox-Fordyce Disease, Relief with Testosterone Presented by DR F E SENEAR and staff

Congenital Syphilis, Second and Third Generation Presented by DR JAMES H MITCHELL and DR RALPH SCULL

Lipomelanotic Reticulosis (Pautrier-Woringer Disease) Presented by DR STEPHEN ROTMAN and (by invitation) DR M J SCHERBER and DR E L LADEN

R L, aged 63, was admitted to St Joseph Hospital in Chicago on April 30, 1947, with the complaints of swelling, redness and weeping of the skin of the

entire body of one year's duration This ailment started with a pruritic dermatitis on the ankles and elbows, which the patient attributed to contact with brick and lime dust In a few months it had spread to involve the entire body He was treated with local applications and injections with only temporary relief During the first six months of the illness the patient lost 26 pounds (12 Kg) in weight

In March 1947, the patient suffered an acute abdominal episode, which was interpreted as thrombophlebitis of the mesenteric veins, followed by generalized peritonitis

On admission to the hospital in April, there was diffuse erythema, swelling and oozing of most of the body The face and large flexures displayed lichenification Pruritus was intense There was generalized lymphadenopathy with single, hard, enlarged lymph nodes The tongue was beefy red and infiltrated, grayish plaques were present between the soft and hard palate The patient was afebrile

The acute manifestations of the dermatitis were checked by local applications When the patient was seen by the consulting dermatologist at this time the impression was erythroderma due to some lymphoblastomas

Laboratory examinations revealed negative serologic reactions, normal urine, erythrocytes 4,000,000, hemoglobin 10 5 Gm and leukocytes 21,000, with 69 per cent polymorphonuclear cells, 13 per cent lymphocytes, 9 per cent eosinophils, 2 per cent monocytes, 1 per cent basophils and 6 per cent stab cells Plasma proteins were 6 5 Gm per hundred cubic centimeters, albumin 2 8 Gm and globulin 3 7 Gm per hundred cubic centimeters with a ratio of 1 1 3 Sternal puncture showed hyperplasia of neutrophil precursors and a decrease in percentage of erythroblasts The left shift of neutrophil precursors was not pronounced enough to permit a diagnosis of myelogenous leukemia It was thought to be a leukemoid reaction Biopsy of the skin and lymph node was performed The microscopic skin sections showed chronic inflammation with a great number of melanophores and large pale cells with vesicular nuclei In the lymph node specimen the cortex is infiltrated by large pale cells, eosinophils, numerous pigmented cells and some polymorphonuclear and plasma cells

During his hospital stay the patient had two attacks of septic thrombophlebitis with positive blood cultures of hemolytic Staphylococcus albus, each time recovering *after penicillin and dicumarol® therapy*

The pruritus was greatly relieved by roentgen irradiations Several blood transfusions were given

During the observation period there has been a conspicuous darkening of the skin leading to the now prevailing color shade The leukocyte count has varied between 10,000 and 25,000 The relative lymphocytopenia has become progressively worse, down to 6 per cent lymphocytes with 88 per cent polymorphonuclear cells and a leukocyte count of 17,200

DISCUSSION

DR HAMILTON MONTGOMERY, Rochester, Minn I wonder whether a new name is needed or whether this should be called a new disease One sees deposition of melanin pigment in the lymph nodes in a great many inflammatory conditions, in association with lymphoblastomas, in psoriasis and also in conditions in which there is excess pigment in the skin In the case presented today the second biopsy simply revealed a nonspecific dermatitis, in other words, this man had an exfoliative dermatitis or generalized erythroderma without evidence of lymphoblastoma There is increased pigment in both the skin and the lymph nodes

DR ADOLPH ROSTENBERG JR (by invitation) As I understand this term, it does not really designate a cutaneous diagnosis It is purely a pathologic term

this "transitional" variety, they may merely be cases undergoing a single transitory tuberculoid reaction In reply to Dr Montgomery's query regarding sarcoid I was not aware that the lepromin test was necessarily negative in sarcoid, or at least in sarcoid not due to leprosy It had been my feeling that in areas where leprosy was not endemic, positive reactions to lepromin would be relatively unusual and that many cases of sarcoid would therefore, in such areas, be fairly likely to have negative Mitsuda reactions—permitting tuberculoid leprosy to be excluded with fair accuracy This situation does not exist in Hawaii, or in any place where leprosy is endemic However, if anergy in sarcoid is expressed in a negative reaction to lepromin as well as in a negative reaction to tuberculin, the problem is greatly simplified In answer to Dr Weidman, I believe that *Nachtblau* cannot be purchased at the present time, but Dr Reenstierna has promised to give me a small quantity of it, and perhaps some more can be obtained through him at the University of Uppsala in Sweden As to the Fite technic, Fite himself has virtually abandoned it in favor of the Feraca procedure, which is certainly far simpler and more rapid and which he believes is equally satisfactory for finding rare organisms My colleague Dr Tilden and I still prefer to see blue-black bacilli against a pale orange-yellow background

clusive toward allying this entity with urticaria They attest to the efficacy of parathyroid extract used in conjunction with calcium in the former, compared with the mediocre results in the latter

SUMMARY

The failure of the antihistaminic or antiallergic agents to influence lichen urticatus favorably is presented as further evidence to disprove any connection of this condition with urticaria

1819 West Polk Street

FATE OF CENTRAL NEVUS IN LEUKODERMA ACQUISITUM CENTRIFUGUM

MORRIS LEIDER, M D
BROOKLYN
AND
ALEXANDER A FISHER, M D
WOODSIDE, N Y

MOST accounts of leukoderma acquisitum centrifugum do not make clear what, if anything, ultimately happens to the central hyperpigmented spots that make this condition so distinctive Neither Sutton,[1] who originally described the picture minutely after Hyde [2] had noted it, nor Leider and Cohen [3] in their recent review discussed the eventual disposition of the moles However, a few of the intervening observers,[4] particularly in the foreign literature, remarked that the central pigmentations sometimes disappear To quote one, Kuske[4c] wrote that " one gets the impression, from history and objective finding, that in some of the lesions undergoing enlargement, the nevus in the center is gradually obliterated by the depigmenting process "[5]

In 1 of Sutton's 2 original cases, the mother of the patient (a child), stated that the central spot had not been present before the onset of the depigmentation In consequence of such observations on the part of patients or their close relatives, some authors have theorized that the pigmented areas in the centers form because melanin, or propigment, drains from the periphery into a centripetal concentration We doubt that these observations are correct and that the resultant theory is

1 Sutton, R L An Unusual Variety of Vitiligo (Leukoderma Acquisitum Centrifugum) Report of Two Cases, J Cutan Dis **34** 797, 1916

2 Hyde, J N Vitiligo with a Central Mole, J Cutan Dis **24** 54, 1906

3 Leider, M, and Cohen, T M Leukoderma Acquisitum Centrifugum, Arch Dermat & Syph **57** 380 (March) 1948

4 (*a*) Gougerot, H, and Carteaud, A Maladie de Sutton avec régression d'un naevus pigmentaire pendent l'accroissement de l'achromie, Bull Soc franç de dermat et syph **41** 1526, 1934 (*b*) Meirowsky, E Leukoderma Acquisitum Centrifugum (Sutton), in Jadassohn, J Handbuch der Haut- und Geschlechtskrankheiten Berlin, Julius Springer, 1933, vol 4, pt 2, p 1000 (*c*) Kuske, H Ueber Leukoderma acquisitum centrifugum (Sutton), Dermatologica **88** 282, 1943

5 The original read " bekommt man durch die Anamnese und durch den objectiven Befund den Eindruck dass bei einigen sich ausdehnenden Elementen auch der Naevus im Zentrum allmahlich dem Depigmentierungsprozess verfallt "

HEREDITARY ANHIDROTIC ECTODERMAL DYSPLASIA

A Clinical and Pathologic Study

BETTE Y UPSHAW, M D
Fellow in Dermatology and Syphilology, Mayo Foundation
AND
HAMILTON MONTGOMERY, M D
ROCHESTER, MINN

THE SYNDROME of hereditary anhidrotic ectodermal dysplasia, which has as its most prominent characteristics anhidrosis, hypodontia or anodontia and hypotrichosis, is one of a group of approximately 200 primarily cutaneous congenital abnormalities that are described in Cockayne's [1] extensive study of this subject Of this group, the following five types of abnormalities were studied and described by one of us (B Y U) in a Mayo Foundation thesis, "Congenital Ectodermal and Mesodermal Dysplasias, A Clinical and Pathological Study" (1) anhidrotic ectodermal dysplasia, (2) hidrotic ectodermal dysplasia, (3) erythroderma ichthysiforme, (4) pachyonychia congenita and (5) Ehlers-Danlos syndrome

In our experience, each and all of these five types of abnormalities can well be called rare, less than 40 patients affected by them have been encountered at the Mayo Clinic in the past twenty-seven years This paper will be confined to the study of the 4 patients affected by anhidrotic ectodermal dysplasia observed at the clinic since 1920

Although, according to Darwin,[2] a description of this syndrome was given by Widderburn [3] in 1838, the term "congenital ectodermal defect" was not used until a case was reported by Christ [4] in 1913 Later observers also used this term until Weech [5] in 1929 designated the

From the section on Dermatology and Syphilology, Mayo Clinic
Abridgment of a thesis submitted by Dr Upshaw to the Faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Dermatology

1 Cockayne, E A Inherited Abnormalities of the Skin and Its Appendages, London, Humphrey Milford, 1933

2 Darwin, C R The Variation of Animals and Plants Under Domestication, New York, D Appleton & Company, 1894, vol 2, p 319

3 Widderburn, W Cited by Darwin [2]

4 Christ, J Cited by Goeckermann [14]

5 Weech, A A Hereditary Ectodermal Dysplasia (Congenital Ectodermal Defect) A Report of Two Cases, Am J Dis Child **37** 766-790 (April) 1929

true Nevertheless, the possibility led Niles[6] to attempt cure of the condition by extirpation of the central spots in the hope of interrupting the assumed attraction of pigment thereto Niles reported failure to influence the depigmenting process by this means Nor did the central pigmentations tend to recur, as one would expect they possibly would if the theory of centripetal drainage of pigment had any virture Moreover, in undisturbed cases, the central nevi or hyperpigmentations according to this theory, should grow larger for as long at least as the process is active This situation we believe and will show does not exist

Leider and Cohen,[3] among many others before them,[7] maintained that leukoderma acquisitum centrifugum is nothing more than banal vitiligo that starts accidentally, or for the particular but unknown reason that causes all depigmentation, around preexisting moles Kuske,[4c] who was previously quoted, expressed disagreement in the following words " Sharply delimited, round or oval, depigmented spots without a visible nevus can readily be confused with true vitiligo At present it appears to me that a distinction [between Sutton's phenomenon and vitiligo] is justifiedly made "[8] Kuske based his conviction on a table of clinical differences which we do not find persuasive

In support of the contention that leukoderma acquisitum centrifugum is merely a variant of simple vitiligo, we report by photographs the following instances of spontaneous disappearance of the central maculopapules while the patients were under prolonged observation We never saw nevi come into being, nor could the patients assert that the nevi had not been present long before the depigmentation had begun We noted established vitiliginous areas increase in size both centrifugally and centripetally, i e, away from and into the hyperpigmented centers and we saw new depigmentations begin around other old nevi The nevi seemed to be invaded by the depigmenting process and were gradually blotted out We can make nothing more of this phenomenon than the usual progression of vitiligo The central hyperpigmented areas persist only so long as it takes the depigmenting mechanism, whatever it may be, to bleach them completely The reason that it takes as long as it

6 Niles, H D Leukoderma Acquisitum Centrifugum, Arch Dermat & Syph **43** 357 (Feb) 1941

7 (*a*) Sutton[1] (*b*) Hyde[2] (*c*) Hebra F and Kaposi, M On Diseases of the Skin Including the Exanthemata, translated and edited by W Tay, London The New Sydenham Society, 1874 vol 3 p 180 (*d*) Stokes, J H Leukoderma Acquisitum Centrifugum (Sutton), Arch Dermat & Syph **7** 611 (May) 1923

8 The original read " Scharf begrenzte, runde oder ovale depigmentierte Herde ohne sichtbaren Naevus konnten leicht mit echter Vitiligo verwechselt werden Zur Zeit scheint mir die Trennung gerechtfertigt

group as "the anhidrotic type of hereditary ectodermal dysplasia," a term which we believe to be most descriptive, because it emphasizes both the cause and the most important clinical symptom of the syndrome, inability to sweat

According to recent reviews of the literature including those of Kaalund-Jørgensen and Christensen [6] and Helweg-Larsen and Ludvigsen,[7] approximately 80 cases of the complete anhidrotic syndrome had been reported prior to 1947 The syndrome has a wide racial distribution, reports having been made from many of the countries of North America, Europe and Asia

Although this triad of symptoms, namely, hypodontia, hypotrichosis and anhidrosis, has been observed many times during the past hundred years, the literature we have read includes no observation of universal anhidrosis that occurred alone This is unusual when one considers that universal aplasia of other single components of the skin, such as hair or pigment to produce alopecia totalis or albinism, respectively, is not infrequent

CLINICAL CHARACTERISTICS

The patients affected by the anhidrotic type of ectodermal dysplasia resemble each other to a remarkable degree because of their unusual facies, which is somewhat suggestive of congenital syphilis and is characterized by high, wide brows, prominent frontal bosses, depressed nasal root and bridge, thick lips with radiating furrows about the mouth, and satyr-like ears

The skin of these patients is unusually soft, thin and feminine Total or almost total lack of sweat gland function under all environmental conditions is the most important physiologic feature, sebaceous gland activity is usually diminished to a variable degree, but apocrine function may be normal The mammary glands may be normal or, as described by Clarke and McCance [8] as well as others, they may be deficient or absent

A delayed appearance and a marked deficiency of development of scalp hair eyebrows and eyelashes and lanugo are frequent, but there is often little uniformity in the degree of development of hair beginning at or after puberty, the beard being more frequently normal, while axillary and pubic hair is either scanty or absent Scalp hair is usually stiff fine and short

6 Kaalund-Jörgensen O and Christensen J F Congenital Ectodermal Dysplasia of the Anidrotic Type, Acta dermat-venereol **22** 1-23 (Feb) 1941

7 Helweg-Larsen, H F, and Ludvigsen, K Congenital Familial Anhidrosis and Neurolabyrinthitis, Acta dermat-venereol **26** 489-505 (May) 1946

8 Clarke R E, and McCance, R A Familial Sex-Linked Ectodermal Dysplasia with Incomplete Forms, Arch Dis Childhood **9** 39-44 (Feb) 1934

does for the central pigmentation to disappear is perhaps that the amount of pigment is so excessive or that nevi resist withering on account of their inherent good capacity to produce pigment Also, it seems to us that the very disappearance of the central pigment in this manner disposes of theories like those of Feldman and Lashinsky [9] and others that leukoderma acquisitum centrifugum is a nevoid disease *sui generis* If one wishes to admit vitiligo as a nevoid anomaly (tardus), then leukoderma acquisitum centrifugum is a nevus, too, but still a variant of vitiligo

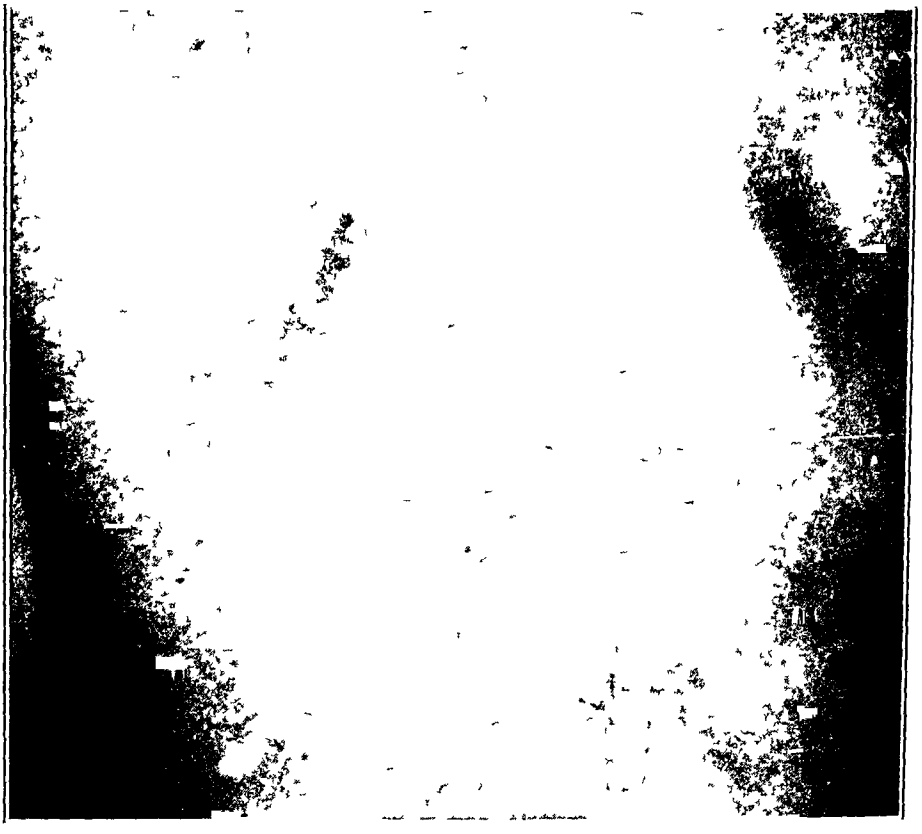


Fig 1 —Leukoderma acquisitum centrifugum, showing lesions with and without central pigmented spots What appears to be residual pigment in some instances is erythema

Figure 1 shows comparable circles of vitiligo, some bearing the central pigmented spots and some lacking them When the patient was first seen by one of us (A A F), almost all lesions bore a nevus Many of these nevi are known, from periodic examination at regular intervals over several years, to have vanished, leaving only the enlarging vitiliginous areas In this case, histologic examination of a site which was

9 Feldman S , and Lashinsky, I M Halo Nevus Leukoderma Centrifugum Acquisitum (Sutton) , Leucopigmentary Nevus, Arch Dermat & Syph **34** 590 (Oct) 1936

The nails of anhidrotic patients are often normal but may exhibit slow growth, longitudinal furrows or slight atrophy

Delayed dentition and hypodontia regularly occur in these patients There is not only a deficiency in number of both deciduous and permanent teeth, but the teeth present are usually abnormally placed and their normal anatomic markings are frequently absent Complete anodontia accompanying anhidrosis has been reported by several authors, including Guilford [9] and Thoma and Allen [10], however, complete roentgenologic proof of anodontia is not given by all of these authors The erupted teeth, particularly the incisors and bicuspids, are often widely separated, peg shaped or conical, darkly pigmented and fragile The development of the maxilla and mandible is in proportion to the number of erupted teeth and usually depends on the amount of resulting mastication made possible, but bony development may be normal in patients with complete anodontia

We have found in the literature no reference to congenital cataracts in connection with this syndrome, although the lens is of ectodermal origin and such an anomaly might be expected Many authors, however, do report deficient function of the lacrimal glands Along with their nasal deformity, many of the patients have chronic rhinitis, often accompanied by nasal discharge of a foul-smelling fluid and diminution of the olfactory sense The glands of the mucous membrane of the nose and throat have repeatedly been found to be deficient in secretory function, producing a decrease in sense of taste, dysphagia, hoarseness and intermittent complete aphonia

Although their anomalies are of ectodermal origin, only rarely have definite defects of the nervous system been found in typical anhidrotic patients It is true, however, that numerous anhidrotic patients have been mentally inferior, but it is commonly believed that the same genetic mutation is not responsible for both of these anomalies

In addition to the aforementioned clinical characteristics which are diagnostic of ectodermal dysplasia of the anhidrotic type, other abnormalities occasionally and probably coincidentally have been associated with it, including skeletal anomalies and dysfunction of the adrenal medulla and the pituitary gland

HISTOPATHOLOGIC CHARACTERISTICS

The majority of observers who have studied excised epidermis from anhidrotic patients have reported either a total absence of sweat glands or the presence of rudimentary fragments of nonfunctioning glands and

9 Guilford, S H A Dental Anomaly, Dent Cosmos **25** 113-118 (March) 1883

10 Thoma, K H, and Allen, F W Anodontia in Ectodermal Dysplasia, [case 38], Am J Orthodontics **26** 503-507 (May) 1940

marked to have had a preexisting nevus at one time, but from which a biopsy specimen was taken after spontaneous depigmentation had occurred, showed absence of nevus cells and only the negative picture of vitiligo When the central spot is an indisputable nevus rather than an ephelis or lentigo, another nice question is that of what becomes of the nevus cells on disappearance of the mole Are they destroyed or are they dispersed? However that may be, we think that any person with as many lesions as these, some adorned with and some bare of

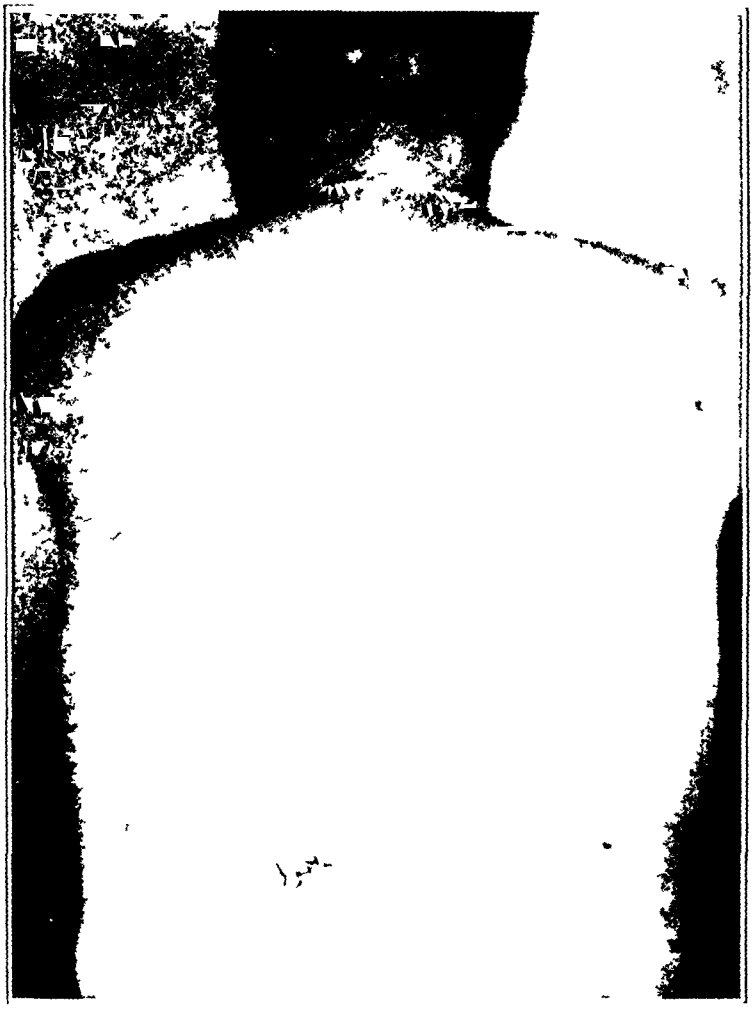


Fig 2—Leukoderma acquisitum centrifugum Compare with figure 1

the central spot, may be assumed to have had more central pigmented maculopapules to begin with, some of which had disappeared by the time the first examination was made This must have been the situation for the patient in case 1 of Leider and Cohen (fig 2) whose photograph shows a nearly identical picture

Figures 3 and 4 are 'before" and after photographs of the patient in case 2 in the article of Leider and Cohen The spontaneous dissolution of the central preexisting nevus was complete What appears in the picture as a pigmented center was erythema, which photographed

ducts There is usually a similar marked deficiency of pilosebaceous structures, but this anomaly is more variable in degree The epidermis is usually thinner than normal, and there is likewise a reduction in width of the cutis, but collagen and elastic fibers and blood vessels are normal in appearance Sunderman [11] reported normal apocrine glands but absent eccrine glands in his biopsy material from the axillas of 2 patients In the anhidrotic patients of Helweg-Larsen and Ludvigsen, as microscopic sections revealed, the number of sweat glands was much reduced, while the glands which were present were hypertrophic

Biopsies of the thin, dry mucous membranes of the mouth and upper respiratory passages have revealed hypoplastic changes in the epithelium as well as in the underlying glands, corresponding with the clinical appearance of these structures

PHYSIOLOGIC CHARACTERISTICS

It must be pointed out that evidence of complete anhidrosis based on single or multiple biopsies is incomplete, even though the sites include the palm or the sole and serial sections reveal no sweat glands Specific physiologic studies of temperature and sweat are necessary for proof of complete anhidrosis At ordinary environmental temperatures and at rest, when the sweat glands are not needed to dissipate heat, the amount of insensible perspiration given off by cutaneous transudation of water is quite sufficient to maintain a normal temperature of the body in anhidrotic as well as in normal patients However, at high environmental temperatures, when a temperature of 98 6 F can be maintained in a normal person by the function of sweat glands, the temperature of the anhidrotic patient rises rapidly to extremes of 102 to 104 F , and the pulse and respiratory rates increase proportionately in a vain attempt to dissipate heat

Although the amount of perspiration of anhidrotic patients is inadequate to maintain a normal body temperature at high environmental temperatures, Felsher [12] has observed that some few sweat glands may be present and functioning in these patients By applying a starch-iodine mixture to the skin of his patients, he saw a few small areas where sweat was being produced when the skin was exposed to heat He therefore suggested that the term "hypohidrosis" rather than "anhidrosis be applied to this group of patients

11 Sunderman, F W Persons Lacking Sweat Glands Hereditary Ectodermal Dysplasia of the Anhidrotic Type, Arch Int Med **67** 846-854 (April) 1941

12 Felsher, Z Hereditary Ectodermal Dysplasia Report of a Case with Experimental Study, Arch Dermat & Syph **49** 410-414 (June) 1944

dark In the flesh it was red and it would show so on a color photograph The interim was eighteen months, and during this period the gradual progressive depigmentation had been noted on several occasions In both of these cases in which we were able to follow the extinction of the nevi, we saw that as the pigmentation faded it left erythema, which then eventually blanched and blended into the surrounding pallor of the vitiligo In addition, whether the original



Fig 3 —Leukoderma centrifugum acquisitum, beginning

pigmented spot was a macule or a papule, the end result was always flat and level with the neighboring skin

It may be argued that the central hyperpigmentations in leukoderma acquisitum centrifugum first come into being because melanin drains to the center, thus forming the moles, and that they then get involved by the "vitiligizing" process which erases them We remember no report in which a medical observer claimed to have witnessed the first event of nevus formation Therefore, it appears much more likely to us that nevi, lentigines and ephelides, which are so common to all, preexist or arise in the ordinary mysterious manner Whenever they come into

ETIOLOGIC FACTORS

Because of the facial similarity of anhidrotic patients and patients with congenital syphilis, clinicians formerly believed the cause of the anhidrotic syndrome to be congenital syphilis Still others explained the syndrome on the basis of endocrine dysfunction, but it now appears that all etiologic concepts other than those of heredity have been disproved

The first anhidrotic patients described by Widderburn,[3] were 10 male members of a Hindu family, and although many patients have been reported who gave absolutely no family history of abnormalities, the majority of patients have ancestors with similar anomalies When the full syndrome is not found in other members of the family, several of them will often have one or more of the component anomalies, except anhidrosis, that comprise typical anhidrotic dysplasia

The exact mode of genetic transmission of the full anhidrotic syndrome has been the subject of controversy since the first cases were encountered It was noted early that males are affected much oftener than females, of the first 60 patients, only 8 were females, according to Kaalund-Jørgensen and Christensen,[6] who also listed 7 instances in which the typical syndrome occurred in siblings Wechselmann concluded from his studies that the defect was transmitted as a sex-linked characteristic, in the same manner as hemophilia, by an unaffected female conductor to affected male members of the family [13] Goeckermann,[14] in a report on a female patient, pointed out that the syndrome was not always recessive in females As more and more cases were reported, it became obvious that the mode of genetic transmission is not identical in all patients Geneticists now emphasize that one peculiarity of human genetics is that the same abnormal character may be sex linked, dominant or recessive in different families, and there are now reports in the literature of the genetic transmission of the complete anhidrotic syndrome by each of these modes of inheritance

PATHOGENIC FEATURES

Although the time and mode of production of the anhidrotic syndrome constitute a subject of much speculation, little detailed information is known

The relative order of normal embryologic development of the dermal appendages which are involved in the syndrome is as follows 1 The hair develops from downgrowths of the epidermis which appear

13 Wechselmann, W, and Loewy, A Untersuchungen an drei blutsverwandten Personen mit ektodermalen Hemmungsbildungen, besonders des Hautdrusensystems, Berl klin Wchnschr **2** 1369-1373 (July) 1911

14 Goeckermann, W H Congenital Ectodermal Defect, with Report of a Case, Arch Dermat & Syph **1** 396-412 (April) 1920

being during life they tend to be permanent They may, relatively rarely, disappear as a result of trauma or other uncertain reasons In leukoderma acquisitum centrifugum they seem to be invaded by the same depigmenting process that concurrently affects the ordinary skin

F Parkes Weber [10] speculatively suggested that there may be a constant law embracing the phenomenon of depigmentation of this sort,

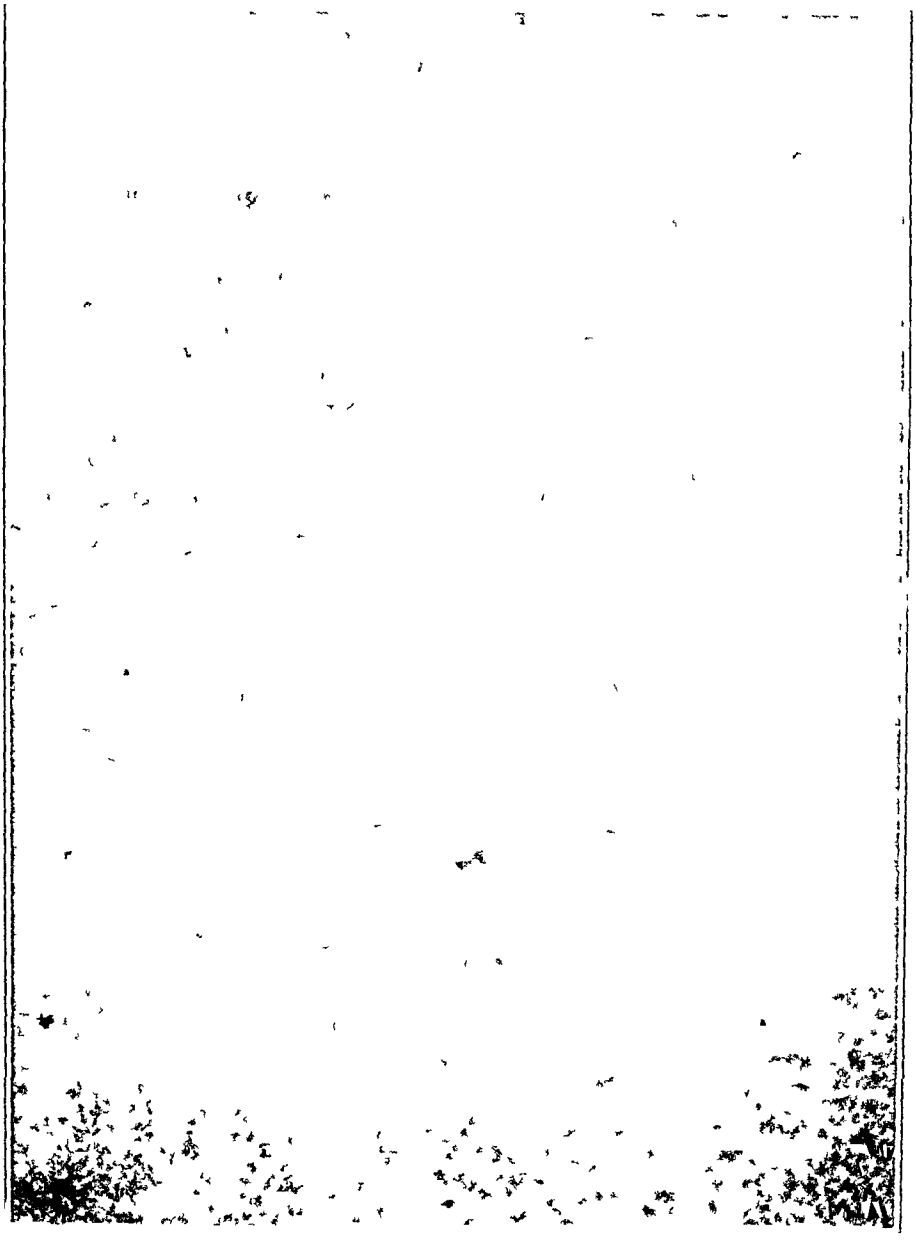


Fig 4—Same case as in figure 3, about eighteen months later The darker portion in the center is erythema, not pigment

as follows Nevi predispose to circumferential depigmentation in an amount that is in direct proportion to their size Stokes [7d] noted, and we have too that leukoderma acquisitum centrifugum is rather common

10 Weber F P A Law Regarding the Distribution of Pigmented (Leucodermic) Patches of Vitiligo, When They Are Superadded to Mole-Like Nevi Brit J Child Dis **21** 202, 1924

between the second and third months of gestation, first in the region of the eyebrows and forehead Between the fourth and fifth months, rudiments of hair begin to grow from these follicles 2 The earliest evidence of nails appears during the third month, but formation of the nail matrix occurs later, at the fifth month of gestation 3 Sebaceous glands originate as lateral outgrowths of the hair follicles during the fifth month 4 Sweat gland anlages appear first on the tips of the phalanges between the fourth and fifth months, and on the proximal portion of the extremities and the trunk by the end of the sixth month, development of these glands is almost complete before birth

The remainder of the embryologic data concerned in the syndrome is as follows 1 The teeth have a double origin, the enamel organ develops from the ectoderm, and the dentine, pulp and cement develop from the mesoderm By the seventh week of gestation, the dental lamina of the ectoderm shows circumscribed thickenings where the future teeth are to be formed At eight weeks, the underlying mesodermal cells begin their growth and differentiation to form the future mesodermal portion of the teeth 2 The milk ridge appears in the embryo between the fifth and sixth weeks of intrauterine life, and from it, in the pectoral region, papilla-like anlages of the mammary glands develop early in the fifth month 3 The neural tube, from which the entire nervous system, the adrenal medulla and a portion of the pituitary gland develop, is completely closed and separated from the overlying epidermis by the beginning of the second month of gestation

Since few reports of definite abnormalities of the nervous system in anhidrotic patients have been recorded, it seems probable that the pathologic process resulting from the defective gene or genes begins to affect the development of the epidermal structures during the second fetal month However, the lens, although undergoing separation from the ectoderm during this time, enjoys, to our knowledge, complete immunity Although the mechanism of genetic transmission of these defects is fairly well understood, at this time the method by which certain structures appear to be haphazardly affected by these genes is not at all clear

Most observers have agreed that the pathologic process is probably an aplasia and not an atrophy because degenerative changes in ectodermal structures rarely have been seen in tissue sections, the structures instead appear never to have begun or just barely to have begun to differentiate

DIFFERENTIAL DIAGNOSIS

There are four diseases which usually have enough symptoms in common with the anhidrotic syndrome to be considered in its differential diagnosis The accompanying table is a brief summary of their essential similarities and differences

if sought for and that non-nevoid conditions, like the lesions of psoriasis, syphilis, Boeck's sarcoid and burns, are frequently surrounded by leukodermatous halos, and he therefore postulated that a common physicochemical inhibition of melanogenesis is at the basis of all such depigmentations It seems to us that hyperpigmentations too are common around many dermatoses, including those mentioned by Stokes, none of which is commonly associated with problems of melanogenesis Coupling our own observations with those of Weber and Stokes, we should say that there may be a law about pigmentary dyscrasia which may be formulated as follows Any abnormality of the skin, congenital or acquired, perceptible or imperceptible, may become a locus of pigmentary disturbance in directions of excessive formation and concentration or of inadequate formation and dispersion When the disturbance is in the direction of depigmentation, is imperceptible and is of point source and unknown cause on apparently normal skin, the clinical picture appears like that of banal vitiligo When the predisposing disturbance, again in the direction of depigmentation, is an obvious lesion, then the clinical lesion may be leukoderma acquisitum centrifugum, with either a nevus or some other non-nevoid condition in the center In the latter event, the word leukoderma is a most proper designation because the depigmentation is related to a known proximate cause In reverse, the very same types of pigmentary disturbances may in other cases eventuate in chloasma-like changes Indeed, vitiligo itself often seems to be accompanied with hyperpigmentation at its border, which observation supports a concept of melanogenesis as a mechanism of such delicate balance that the very same influence, or train of influences, seems to be able to direct it into the direction of either hypopigmentation or hyperpigmentation or of both simultaneously

820 Caton Avenue (18)

4514 Forty-Eighth Street

TREATMENT

Treatment of anhidrotic patients is largely symptomatic because of the fundamentally aplastic lesions of the syndrome, but certain therapeutic principles should be emphasized to the patient or to the parents of an anhidrotic infant The limiting effect of the anhidrosis on the mode of living must be well understood, the genetic transmission of

Differential Diagnosis of the Anhidrotic Syndrome

	Anhidrotic Ectodermal Dysplasia	Hidrotic Ectodermal Dysplasia	Werner's Syndrome	Rothmund's Syndrome	Progeria, Hutchinson Gulliford Type
Genetic transmission	Dominant, recessive or sex linked	Usually dominant	Usually recessive	Usually recessive	Not proved
Age at onset of symptoms	First year	First year	20 to 30 yr	1 to 5 yr	1 to 5 yr
Facies	Inverted pyramid, frontal bosses, depressed nasal bridge	Not characteristic	Senile changes, beaked nose, small mouth and chin	Not characteristic	Frontal bosses, beaked nose, retracted chin
Skin	Dry, soft, feminine	Hyperkeratoses of palms and soles, oriental pigmentation	Epidermal, subcutaneous and muscular atrophy of distal extremities with trophic ulcers	Atrophy, brownish pigmentation, telangiectases	Atrophy of epidermis, subcutaneous tissue and muscle
Sebaceous glands	Markedly decreased	Slightly decreased	Normal	Normal	Normal
Sweat glands	Decreased or absent	Normal	Normal	Normal	Normal
Mammary glands	May be absent	Normal	Normal	Normal	Normal
Hair	Generalized alopecia, usually subtotal	Generalized alopecia, always subtotal, fragile hair	Canities and premature alopecia	Usually normal	Premature alopecia
Nails	Normal	Short, thick, elevated tip	Normal	Normal	Short, fragile
Teeth	Decreased or absent, also deformed	Normal	Normal	Normal	Irregular development
Eyes	Normal	Normal	Juvenile cataracts	Juvenile cataracts	Normal
Systemic abnormalities					
1 Cardiovascular	Distinct intolerance of heat	None	Early arteriosclerosis	None	Early arteriosclerosis
2 Skeletal	None	Usually none	Short stature, osteoporosis	Occasionally short stature and small hands and feet	Dwarfed trunk and extremities, joint deformity
3 Endocrine	Usually none	Pituitary and suprarenal deficiency (?)	Hypogonadism, diabetes	Occasional hypogonadism	Hypogonadism
Prognosis for life	About average	Average	Death before age of 40 yr	Average	Death before age, of 30 yr

the defect should also be explained, and no assurances should be given to the parents of an anhidrotic child that future children will be normal

Artificial dentures should be fitted early in anhidrotic children with hypodontia to facilitate the development of the mandible and the maxilla Plastic repair of the saddle nose deformity will likewise do much to improve the patient's facies and general morale Mortimer, Wright

IS LICHEN URTICATUS A FORM OF URTICARIA?

THEODORE CORNBLEET, M D
CHICAGO

SINCE the time of Bateman, who accurately described lichen urticatus, there has been controversy about the nature and pathogenesis of this disorder In successive periods of dermatologic history new ideas have developed about this disease, reflecting the thoughts and subject matters current at the moment Thus, at one period, foods and bowel disturbances were said to be causative, in harmony with the emphasis placed on intestinal putrefactions and toxemias At present lichen urticatus is mostly thought of as a form of urticaria, in keeping with the keen awareness of the phenomena of allergy, and is so classified in the textbooks

There has been so much written on lichen urticatus that there would seem to be little excuse for still further overtaxing what has been for the most part theoretic discussion Only new evidence can be an adequate reason for reopening the subject The recent development and use of the antihistaminic or antiallergic synthetic drugs may permit one to survey the problem from a fresh perspective Toward that end the following several case histories are presented

CASE HISTORIES

1 T K R, a Negro girl 4 years old, had a papular eruption mostly on the extensors of the extremities and a few lesions on the trunk and the face, which was diagnosed as lichen urticatus The mother said it was present the previous two summers, too After three weeks' use of diphenhydramine hydrochloride (elixir benadryl hydrochloride®) there was no improvement in the appearance of the lesions or apparently in the distress caused by the itching There was marked betterment after three more weeks during which she was treated simultaneously with parathyroid injection U S P and calcium lactate

2 Z P, a boy 5 years old, had an eruption which had been present in the same form the previous year It was thought to be lichen urticatus Four weeks' use of diphenhydramine hydrochloride failed to produce any evident improvement in the lesions, even though the child slept better and was more restful

3 J O M, a woman 23 years old, had a pruritic papular eruption on the extensors of the arms and legs and scattered elements on the trunk Some of the lesions were acuminate and there was severe pruritus There was no grouping, nevertheless, she was given a course of sulfapyridine treatment on the pos-

From the Department of Dermatology University of Illinois College of Medicine, Service of Dr I E Sonear

and Collip[15] have reported favorably on the results of using estrogenic substances incorporated in a nasal spray in treating anhidrotic patients for chronic rhinitis or ozena In view of the normal longevity enjoyed by the patients affected by anhidrosis, the aforementioned measures, although not curative, are certainly important in making life more pleasant

REPORT OF CASES

CASE 1.—A white boy, 7 weeks of age, was brought to the clinic during warm weather because of intermittent fever that had been present since 2 weeks of age The baby weighed 6 pounds 8 ounces (2,950 Gm) at birth and appeared normal Except for the fever of unknown origin, there were no symptoms of illness The family history revealed numerous congenital abnormalities, none of which could be related to the anhidrotic syndrome The child had no siblings, and there was no history of intermarriage of relatives

In the physical examination the only abnormal findings were absence of eyelashes and eyebrows, and very dry skin over the entire body In the hospital it was noted that the child never perspired and that his temperature increased directly in relationship to the external environment After fifteen minutes under a heat cradle, the rectal temperature rose from normal to 100 F, increases in temperature were noted after each meal No teeth were visible on roentgenologic examination Routine laboratory investigations revealed moderately severe hyperchromic anemia A biopsy specimen was removed from the sole of the left foot, and the multiple sections studied revealed complete absence of sweat glands and ducts, the epidermis and cutis being normal in other respects

Four years later the mother said that no sweating had ever been noted and that by living in the basement during hot weather he had been quite comfortable and able to maintain a normal temperature At 18 months of age he had two pointed teeth which were still present and strong at the age of 4 years His scalp hair was white sparse and slow growing, he had normal eyelashes but no eyebrows The mucous membrane of his nose was dry and crusted, and he had had several severe laryngeal infections, one of which had necessitated tracheotomy His mental development was thought to be normal

CASE 2.—A white boy, 2 years old, was brought to the clinic from a warm climate by his paternal grandmother who said that since shortly after the birth of the child it had been noted that his temperature rose when he was placed in a warm environment The patient weighed 5 pounds (2,270 Gm) at birth, six hours after this event his temperature reached 106 F Fever continued almost constantly during the first summer, and no cause could be found When cool weather began, the child's temperature returned to normal, but it began to rise on the first warm day of the following year His pupils had been dilated since birth, they did not become smaller in the bright sunshine, and photophobia was obvious The child had had eczema of scalp, hands and feet since 6 months of age, and this was much more severe in warm weather When the teeth appeared, they were brown and fragile and soon became carious At 1 year of age, eight teeth had developed The nails had been normal until 1 year of age, when they became rough and scaly The child sat alone at 8 months and walked at 18 months

15 Mortimer, H, Wright, R P, and Collip, J B Atrophic Rhinitis The Constitutional Factor, And the Treatment with Œstrogenic Hormones, Canad M A J **37** 445-456 (Nov) 1937

sibility that the eruption was dermatitis herpetiformis There was no good effect from this therapy She was then given 300 mg of tripelennamine hydrochloride (pyribenzamine hydrochloride®) daily for ten days without visible or subjective improvement Itching largely subsided and much of the eruption was gone after a month of the use of parathyroid injection U S P and calcium lactate

4 D A, a white boy 8 years old, had a papular eruption mostly on the extensor surfaces of the extremities A few lesions had puffy bases, and a frank wheal was present at one site There was itching He was thought to have lichen urticatus The lesions remained largely unchanged after two weeks' use of diphenhydramine hydrochloride

5 C N, a Negro girl 6 years old, had an itching eruption which was believed to be lichen urticatus Three weeks' use of diphenhydramine hydrochloride effected no apparent improvement in her cutaneous condition

COMMENT

The greatest success attending the use of the antihistaminics has been in connection with urticaria It is reasonable to assume that if lichen urticatus is a form of urticaria peculiar to children it should react somewhat similarly to therapeutic agents which benefit patients with urticaria This small series of patients derived no benefit from the newer antiallergic agents in contrast with the happier results commonly seen in ordinary urticaria This raises again doubts that lichen urticatus is primarily an urticarial process Pruritus is common to both, but is present, too, where there is no suspicion of urticaria The mere presence of wheals as one of the primary lesions should not be binding to a diagnosis of urticaria It would seem tenuous to make their presence in urticaria pigmentosa a proper cause for including the latter among the urticarias even though its origin remains unknown Wheals may at times be found in diverse entities, even as the initiating event of a folliculitis or a furuncle

Walzer and Grolnick,[1] in an intensive study of lichen urticatus, employing modern methods of dealing with allergy, were unable to relate this disease to such a process Pillsbury and Sternberg [2] said

> the theory that the nature of this disease is allergic has been commonly held, and most investigations have been concerned in the attempt to prove or disprove this contention We believe that the evidence supporting such a view is extremely meager and that further study along the lines of allergy, unless some unique approach is devised, will probably be fruitless

They reviewed the studies of various authors whose work had failed to resolve the beclouded pathogenesis of lichen urticatus and been incon-

1 Walzer, A, and Grolnick, M Relation of Papular Urticaria and Prurigo Mitis to Allergy, J Allergy **5** 240, 1934

2 Pillsbury, D M, and Sternberg, T H Lichen Urticatus (Papular Urticaria) Treatment with Parathyroid Extract, Theoretical Consideration of Etiology, Am J Dis Child **53** 1209 (May) 1937

The family history revealed no congenital abnormalities, but the patient's paternal great-grandfather and maternal great-grandmother were brother and sister The patient's one sibling, a sister of 8 months of age, was said to have the same abnormalities of eye and temperature as were noted in the patient

On physical examination, the child appeared to be well developed and nourished The facies and the hair distribution were not unusual, but the skin was dry, and no sweating was noted No eczematoid lesions were present, and the teeth and nails were as described The pupils were equal and semidilated and did not react to light Pupillary dilatation did not occur after local instillation of homatropine hydrobromide nor constriction after instillation of physostigmine salicylate or a pilocarpine salt There were pupillary remnants in both eyes, and the fundi were normal The remainder of the physical examination revealed no significant findings, and the laboratory examinations gave essentially normal results

Further observations of the child revealed that his temperature increased after eating and with crying but could be easily controlled by sponging him with cool water After administration of pilocarpine there was flushing of the face, neck and breast down to a sharp line at the nipple level, but no sweating occurred Biopsy of the skin was not performed

When the patient was 5 years old, the grandmother stated that he still was intolerant to heat, that there was no change in his pupils and that his deciduous teeth were black stumps except his six year molars, which appeared normal No sweating had ever been noted in the patient's younger sister, and although she had a complete set of deciduous teeth, they were darkly pigmented and sensitive to sweets, heat and cold

CASE 3.—A white man, 26 years of age, unmarried, working as lifeguard, first came to the clinic during warm weather because of lack of perspiration, scanty growth of hair and abnormal dentition These abnormalities had been present since birth, and the father stated that the patient's abnormalities were familial in character, originating many generations ago in the patient's mother's family, always appearing in one male of each generation and completely absent in the women of the family as far as he knew

Physical examination revealed a well nourished man of average adult size, the ears were protuberant, the root of the nose was depressed and the septum was irregular, but there was no widening or saddle nose deformity The skin was soft and dry On the scalp there was only a sparse peripheral fringe of hair, there was little lanugo over the trunk and extremities, and only a few small tufts of hair in the pubic and axillary regions Two teeth were present, one of which was a small tag There was moderate atrophy of the mucosa of the nasopharynx, pharynx and larynx, but the voice was normal

Biopsy and other laboratory procedures were not performed until the patient was admitted to the clinic a second time, five years later Then it was found that after strenuous physical exercise the rectal temperature increased 2 degrees F His basal metabolic rate was normal on two occasions, but after strenuous exercise it increased to + 40 per cent, while the metabolic rate of the normal control person increased to + 20 per cent After his second admission, histologic examinations were made of skin tissues removed from the right axilla and the lower right part of the thorax, in the serial sections no trace of hair follicles, sebaceous glands, sweat glands or apocrine glands could be found

CASE 4.—A 23 year old unmarried farmer came to the clinic because of weakness of the arms and legs and loss of consciousness, usually occurring just preceding a meal or several hours afterward These symptoms began suddenly during one hot day of the preceding summer and continued to recur during cooler weather He

Hurwitt (*J Invest Dermat* **5** 197 [Aug] 1942) reviewed all the lymph nodes taken out at the Mount Sinai Hospital, New York There is a reticulum and histiocytic cell replacement of the lymphocyte in the lymph node It is purely a benign process and is not related to lymphoblastoma Hurwitt also criticized the term Pautrier-Woringer disease and used the name dermatopathic lymphadenitis About a year later there was an article by Larkin and his co-workers (*J Pediat* **24** 442 [April] 1944) on this same syndrome, with reference particularly to infantile eczema He pointed out that involvement of the lymph nodes is not uncommon in infantile eczema and that these nodes can have a resemblance to those seen in Hodgkin's disease He warned against confusion with manifestations in Hodgkin's disease because this condition is benign

DR S W BECKER I have been of the opinion that this reaction was of a nonspecific variety Someone, some months ago, said that the pathologist at Cook County Hospital considered it a definite entity

DR S M BLUEFARB The original article on lipomelanotic reticulosis was written by Pautrier and Woringer in 1932 (*Bull Soc franç dermat et syph* **39** 947, 1932) They described 6 cases in which the three cardinal signs were exfoliative dermatitis, superficial generalized lymphadenopthy and pigmentation of the skin At that time no specific causative factor was mentioned In a second communication in 1940 Pautrier and Woringer described a case of generalized erythroderma in which typical lesions of mycosis fungoides developed and in which the original lymph node biopsy showed the appearance of lipomelanot c reticulosis and a subsequent one a reticulum cell proliferation found in mycosis fungoides They suggested that there might be a causal relationship between the two conditions At the February 1945 meeting Dr Oliver (ARCH DERMAT & SYPH **54** 621 [Nov] 1946) showed a case of generalized erythroderma with lipomelanotic reticulosis Several months later the patient died of mycosis fungoides

There appear to be several schools of thought regarding the outcome of this disease Dr Rostenberg just mentioned the benignity of this disease I believe that Robb-Smith of England also favors the concept of a benign condition as the patients in the 3 fatal cases in his series appeared to die from intercurrent disease rather than from the skin condition (*Brit J Dermat* **56** 107 [May-June] 1944) However, I do not believe that the disease in all these cases can be considered benign and that one should give a guarded prognosis because in a certain percentage of these cases one of the lymphoblastomas will develop

DR STEPHEN ROTHMAN I share the skeptic attitude of Dr Montgomery concerning the assumption that this is a separate entity On the other hand, the microscopic picture of the lymph nodes is not one of banal chronic inflammation, because the infiltration is invasive, neither does the picture correspond with that of any of the known lymphoblastomas When first seen, this patient had erythroderma with lichenification

Mycosis Fungoides Treated with Sodium Paraaminobenzoic Acid Presented by DR JAMES H MITCHELL

Mrs L McC, aged 52, was presented at the meeting of May 21 At the suggestion of Dr Arthur Curtis, treatment with sodium paraaminobenzoic acid was begun March 29, 1947 Tablets of 2 Gm were taken every three hours during the waking hours The clinical improvement was at first spectacular, but there has been little change in her condition in the past month

DISCUSSION

DR JAMES H MITCHELL The patient was shown last month, and I asked her to come here especially for examination by Dr MacKenna I might say that since she was last presented she has made less progress than she made previously Dr Ormsby pointed out that many different medicaments could improve mycosis fungoides temporarily, and perhaps this medicament will fit in with what Dr Ormsby has said I have another patient treated by the same method and a third one with leukemia It remains to be seen whether we have anything worth while

NOTE—The patient with lymphatic leukemia died without making a satisfactory trial of the medicament The other 2 patients are still doing well

A Case for Diagnosis (Alopecia Areata? Atrophic Glossitis? Acquired Anhidrosis?) Presented by DR FRANCIS W LYNCH

Miss G L, aged 24, first had a dermatologic condition at the age of 14, when she had a febrile illness, possibly rheumatic fever, followed by a generalized eruption which was first regarded as scarlet fever The eruption recurred three times, accompanied with fever and followed by exfoliation After the last febrile attack the exfoliation continued, accompanied with pyogenic infection especially on the hands, feet and scalp, resulting in loss of the nails and alopecia There was also otitis, conjunctivitis and gingivitis About that time the skin on the chest and abdomen became inflamed and was wiped off easily, leaving a moist red surface which subsequently healed The patient was bedridden seven months She lost 67 pounds (30 Kg) in weight

Subsequently there has been persistent alopecia which is almost total There is photophobia and a severe refractile error There was amenorrhea for one year, but the menses again became normal During hot weather she perspires slightly and becomes weak, and her temperature rises to 103 F or more

The family history is normal except that one sister had eczema in infancy The patient has had occasional urticaria

The scalp is almost bald, with some occipital hair remaining There are a few hairs in the lashes and brows, the body and extremities are without hair The bulbar conjunctivas are slightly red and the palpebral conjunctivas show some pale areas and other inflamed areas (They previously were treated by electrosurgery) The tongue presents superficial atrophy The left buccal mucous membrane shows an irregular area of thickening and possibly scarring All the nails are atrophic and deformed The palms and soles are dry and appear to be scarred The extremities are smooth and hairless, and the skin of the legs is thin There are numerous irregular brown macules on the face and hands

DISCUSSION

DR S W BECKER This is an odd case It started out at the age of 14 when the patient had a severe febrile reaction, during which she lost her hair I suppose it was on a systemic basis Later she had a recurrence of the generalized eruption, which she said looked like scarlet fever It recurred a great many times She had a severe crusting eruption of the scalp She obviously has a certain amount of cutaneous scarring, which I presume resulted from the inflammatory reaction She lost not only her hair but her finger nails as well Her tongue is somewhat atrophic, and I thought that there was a little leukoplakia on the tongue and buccal mucosa The palms and soles were peculiar in that she had fungated keratoses which were a little suggestive of an arsenical keratosis I questioned

had had no convulsions at any time and had noted no aura prior to loss of consciousness The patient had been told elsewhere that he had congenital absence of the sweat glands, and he had noted heat intolerance all his life He did not relate the onset of weakness or unconsciousness to becoming overheated or to hyperventilation The family history concerning congenital defects did not disclose anything that was significant Two brothers had died in early infancy of unknown causes

Physical examination revealed a young man of average height and weight (fig 1) His forehead was extremely high, his small eyes were widely separated His nose was wide, the bridge being almost flat The lips were thick and muscular, there was total anodontia, and the mandible and the maxilla were underdeveloped, producing a "dish face" deformity

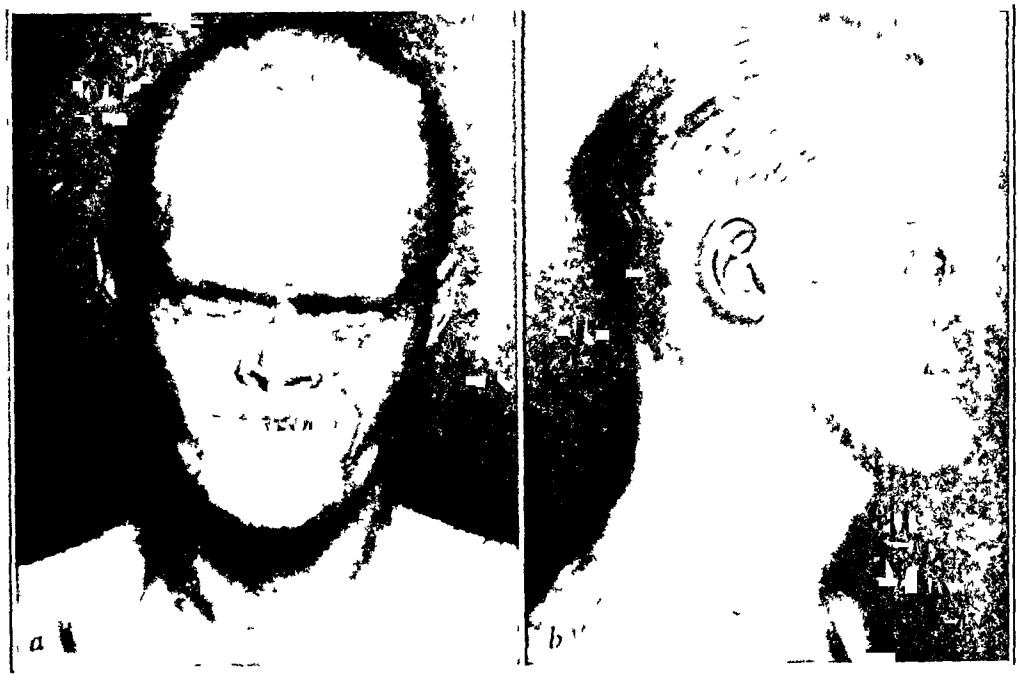


Fig 1 (case 4) —(*a*) Anterior and (*b*) profile views This is the characteristic concave facies of hereditary anhidrotic ectodermal dysplasia Note the sparse growth of hair on the scalp and the normal amount of lanugo in the shoulders

No activity of sebaceous or sweat glands was noted anywhere on the skin, which was excessively dry A diffuse symmetric keratoderma covered the palms, the soles and the nails were normal

There was considerable alopecia of the scalp, most prominent over the vertex The scalp hair present was stiff and dry, and only a few hairs were present anteriorly Eyelashes and eyebrows were absent, and only a few sprigs of hair were present in the axillary and pubic regions The beard was normal, as was the lanugo on the thorax and the shoulders, but lanugo was absent elsewhere

The mammary glands were absent, and there was no pigmentation to mark their usual site No teeth were present The eyes and the lacrimal glands were normal

The thin septum of the nose contained no cartilage, and the mucous membrane was atrophic The senses of smell and taste were intact

by the flea as he bites Or, to put it in other words, a flea may bite, and as a result there may be urticarial lesions at sites remote from the bitten areas

The history is equally important If the sufferer is adult, he is usually new to the Bay region He has been subject to flea bites for only a sufficient period of time to become sensitized by the antigen Most patients suffering from flea bites are children, newly born or newly arrived in the Bay area

Other types of eruptions which are seen more rarely are secondary bacterial infections and other complications of scratching Recurrent

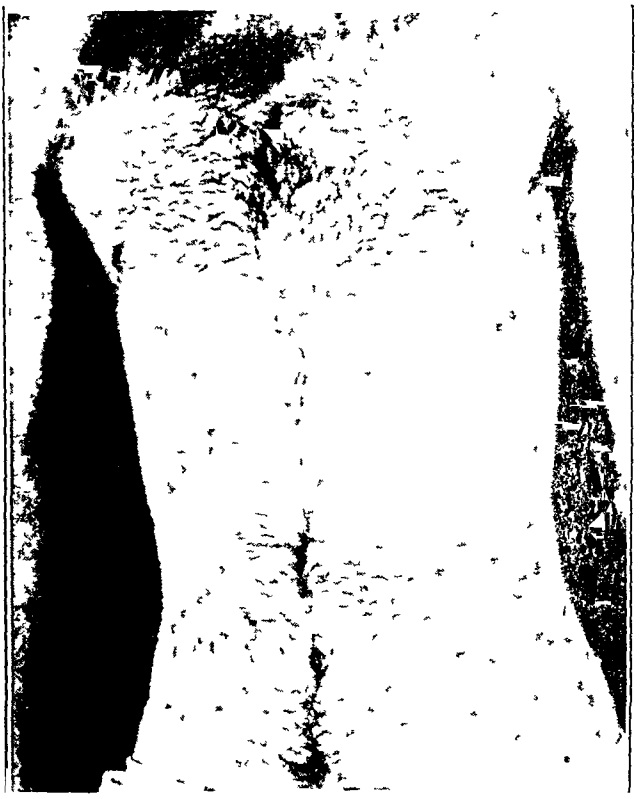


Fig 4—Typical flea bites Note resemblance to papular urticaria (Courtesy of Samuel Ayres Jr, M D, Los Angeles)

furuncles, especially in children, have been observed Less frequently occur bullous eruptions on the lower extremities and generalized, erythema-multiforme-like, bullous eruptions

DIFFERENTIAL DIAGNOSIS

It is the experience of those in our office that most cases diagnosed as "papular urticaria" in our district are in reality examples of flea bites Chipman [4] recognized this fact long ago While my associates and I do

4 Chipman, E D Urticaria, with Special References to the Cause in the Papular Forms of Children, California State J Med 8 207 (June) 1910

Routine examinations of blood and urine gave normal results, as did determinations of the basal metabolic rate and the fasting blood sugar, calcium and potassium Roentgenograms of the skull and the thorax did not disclose any abnormality, and the electroencephalogram revealed mild generalized dysrhythmic activity without localizing signs

Under an electric baker the patient's oral temperature rose from 98 2 to 100 4 F in fifteen minutes After an injection of 5 mg of furfuryl trimethylammonium iodide (furmethide®) flushing and weakness were noted, but no sweat, and no tremor or unconsciousness developed



Fig 2 (case 4) —Section of a biopsy specimen removed from the palm It shows complete absence of sweat glands and ducts (hematoxylin and eosin, × 25)

Biopsy specimens were removed from the skin of the right forearm, right arm and palm of the right hand, in the serial sections no trace of coil glands or ducts was visible (fig 2)

Over a period of several months, three plastic procedures employing cartilage implants succeeded in forming an elevated nasal bridge, so that the patient's appearance was improved Diphenylhydantoin sodium (dilantin sodium®) was prescribed in an attempt to control the episodes of weakness and unconsciousness, the patient was advised to restrict his strenuous farming activities during hot weather

not deny the existence of true papular urticaria of endogenous origin we are certain that it is rare in comparison with the exogenously flea-produced variety Children, particularly, or adults who are newcomers to the Coast are sometimes referred to us by pediatricians or general physicians, with the diagnosis of "hives" The story will invariably be that the patient had not been subject to hives prior to coming to the Coast and that the eruption appeared shortly after arrival here Usually the physician or the patient considers the condition to be an allergy to some of the foods of the West Coast, such as sea foods or fruit It takes a great deal of persuasion for one to convince these patients that the origin of the eruption is not what they are eating but, rather, what is eating them Although this fact is known to all the local dermatologists, it is astonishing that it is not known to all physicians and to the laity

This failure to recognize such a simple, obvious thing as flea bites is not limited to our locality The Jadassohn [5] school in Germany, Hallam,[6] Tate,[7] and Kinnear [8] in England and Urbach [9] in Vienna reported that papular urticaria in children disappeared when the patients were hospitalized and recurred when they returned home Reasoning from this information the English observers [10] and Urbach [9] expressed the conclusion that papular urticaria is an allergic manifestation, the exciting cause of which is something in the home environment, food or bedding These authors made little or no mention of the possibility of fleas or other insects being etiologic factors One of Jadassohn's pupils, Gerard Simon,[5] described a case of prurigo which cleared while in the hospital and had an exacerbation when the patient returned home Hallam [6] quoted Jadassohn to the effect that he had noted many years ago that cases of Hebra's prurigo cleared up when the patients were hospitalized Although the evidence against fleas in these older reports is uncertain, the possibility should be considered In recent reports the evidence against fleas is much stronger Hallam [6] reported a series of patients with papular urticaria whose condition cleared on hospitalization only to relapse on their return to their homes He concluded that papular

5 Simon, G Beitrage zur Kenntniss der "Neurodermitiden," Bern, Stampfli & Co, 1898

6 Hallam, R Further Observations on the Aetiology of Papular Urticaria (Lichen Urticatus), Brit J Dermat & Syph **44** 117 (March) 1932

7 Tate, B C Papular Urticaria (Lichen Urticatus), Arch Dis Childhood **10** 27 (Feb) 1935

8 Kinnear, J Urticaria Papulosa, Brit J Dermat & Syph **45** 65 (Feb) 1933

9 Urbach, E Skin Diseases and Nutrition, Including the Dermatoses of Children, Vienna, Wilhelm Maudrich, 1932, p 175

10 Hallam [6] Tate [7] Kinnear [8]

COMMENT ON CASES

As in case 1, it is not uncommon for anhidrotic infants who have increased temperature shortly after birth to be extensively and vainly studied for evidence of infections Seldom is the correct diagnosis made in the first few weeks of life, and so the child is not subjected to varied and multiple therapeutic methods In contrast to those in adults, the obvious clues to the correct diagnosis, namely, anodontia and hypotrichosis, are normal findings at this age The typical anhidrotic facies, although observed as early as 1 year of age, is not conspicuous in the first few weeks of life, and in the absence of a history of similar hereditary anomalies, unless the family or the physician notes that the rise of temperature is correlated with the external environment, the diagnosis may be delayed until lack of teeth and hair is noted in the second six months of life In case 1, since the patient fortunately was examined in August, the correlation of high body temperature and high external environmental temperature was noted, when, in further study of this phenomenon, the patient was exposed to a heat cradle and no sweating was produced at an abnormally high body temperature, only the biopsy showing absence of sweat glands on the sole of the foot was needed to confirm the diagnosis The absence of teeth on roentgenologic examination of the mandible and the maxilla was further evidence of the existence of the complete anhidrotic syndrome In the child's subsequent development, the repeated infections of the upper part of the respiratory tract illustrated one of the common complications resulting from the abnormal formation of the mucous membrane

Of particular interest in case 2 were the pupillary abnormalities and the mode of inheritance of the syndrome, the latter factor being unknown in case 1 The inability of the pupils to respond to any type of physical or chemical stimuli was thought to be due to defective innervation, though the site of this abnormality of the nervous system could not be determined in absence of other neurologic signs or symptoms This anomaly appears to be one of the rare examples of abnormalities of the nervous system that accompany the complete anhidrotic syndrome

In case 2 all of the patient's manifestations of anomaly were said to be duplicated in his only sibling, a sister, 8 months old When one remembers that the children's parents had common great-grandparents each of which may have carried the anomaly as a recessive genetic character, it is easy to understand why marriage between their descendants resulted in defective children These are obviously homozygous for the causative gene, and this recessive gene was concealed

urticaria is an allergic manifestation, the exciting cause of which is associated with home sleeping arrangements and can be controlled by detaining the child in the hospital for the night only Kinnear [8] described 14 cases of papular urticaria in children which began on their arrival in England from America and said that other cases occurred in their families He had also observed that same occurrence in newly arrived medical students He agreed with Hallam [6] that this condition had something to do with home sleeping conditions He had no idea of the cause and made no mention of the possibility of flea or other insect bites Tate [7] said, "The exciting agent is something connected with the patient's home environment"

My associate, Dr H J Templeton,[11] personally observed many cases of "papular urticaria" in Vienna He reported that patients with so-called papular urticaria suffered from typical flea bites and that their lesions would have been so diagnosed by any of the West Coast dermatologists He observed this "papular urticaria" developed in members of his own family and also in persons in the families of other American physicians and that the lesions were typical flea bites That the diagnosis was not shared by all Viennese dermatologists is evidenced by Dietrich's [12] discussion in which he stated that the cases were really examples of insect bites It is my belief that this confusion occurs in many cases in the literature

Urbach [13] devoted eight pages to the idea that most cases of papular urticaria are of allergic, endogenous or gastrointestinal origin and only two lines to cases in which insects were the cause His photographs 347 and 353 [13] are highly suggestive of bites In another text [9] he showed a photograph of papular urticaria which looks to me like insect bites Macleod's text [14] has a photograph which is almost certainly one of flea bites, with the puncta, papules, grouping and location A photograph in Andrews' text [15] needs to be differentiated from one of flea bites At a clinical meeting of the American Dermatological Association [16] a 3 year old child was presented from Canada as having an example of papular urticaria In the discussion Ayres and Weiss diagnosed the

11 Templeton, H J Personal communication to the author

12 Dietrich, A Lichen urticatus exogenes, Wien klin Wchnschr **50** 1730 (Dec 17) 1937

13 Urbach, E, and Gottlieb, P M Allergy, New York, Grune & Stratton, Inc, 1943, pp 884-891

14 Macleod, J M H Diseases of the Skin, New York, Paul B Hoeber, 1924, p 698

15 Andrews, G C Diseases of the Skin, Philadelphia, W B Saunders Company, 1930, p 348

16 King-Smith, D , Trow, E J, and Dixon, H A Urticaria (Papular), Arch Dermat & Syph **25** 172 (Jan) 1932

until the consanguineous marriage by a dominant normal gene, that was absent in these two children Progeny of heterozygous parents would be expected to show a 1 3 ratio of defective to normal children, but this ratio often becomes apparent only in large families or in long family pedigrees

In case 3 a sex-linked recessive gene was responsible for the defect, according to the father of the patient, since only one male of each generation was affected In contrast, in case 4 we were unable to trace the anomaly at all One must conclude that the condition in this case represents a mutation, and the patient's progeny should be followed with interest to note the genetic transmission of the defect

The facies of the 2 adult anhidrotic patients (cases 3 and 4) is characteristic of the entire group Although in case 3 the patient did not have a saddle nose such as that described in case 4 and frequently described in the literature, the root of his nasal bridge was sharply depressed Both patients presented decided hypotrichosis, complete anhidrosis and hypodontia or anodontia to complete the full anhidrotic syndrome

The anhidrotic syndrome had limited the heat regulation in case 3 to such an extent that the patient's employment as a lifeguard was one of the few types of work which he could carry on in the summertime In case 4 the patient's activity was voluntarily restricted, but he was able to continue farm work in a northern state during almost the entire year We were unable to relate the cause of his periods of weakness and unconsciousness directly to increase in body temperature, but it was felt that a subthreshold cerebral dysrhythmia was made manifest either by the rise in temperature or by the hyperventilation or by both factors

These patients (cases 1, 3 and 4) were all of interest from the standpoint of histopathologic study In none of their biopsy specimens were we able to find sweat glands or sebaceous glands In case 3 the apocrine glands were also absent from the axillary skin examined This is in contrast to the reports of Sunderman,[11] whose patients had apocrine glands but no eccrine glands, as shown by microscopic examination The apocrine glands develop from anlages of hair follicles instead of directly from the epidermis as do sweat glands, in the embryo, and do not become active until near puberty The presence of highly developed apocrine glands and the sparse growth of hair, on one hand, and the absence of sweat glands, on the other, illustrate the complete suppression of the sweat gland formation and the incomplete suppression of pilosebaceous structures which are peculiarly characteristic of the anhidrotic syndrome

case as one of insect bites In the *British Journal of Dermatology and Syphilis* [17] a reviewer wrote of "papular urticaria (a condition furtively believed by not a few since Jonathan Hutchinson to be produced by insect bites) " Jonathan Hutchinson [18] expressed the opinion that fleas had something to do with the lesions "It may be that flea bites acting on a skin sensitized by faulty alimentary metabolism is the determining cause" Concerning the first step in treatment MacKenna [19] said, "Inquire judiciously into the possibility of infestation with fleas"

From all this evidence, I conclude that elsewhere in the world there is the same problem of differentiating papular urticaria from flea bites that exists on the West Coast



Fig 5—Histologic aspects of the flea bite Note the intensity of the reaction

PATHOLOGIC ASPECTS

A flea bite papule was excised from each of 5 patients for microscopic examination Each of these lesions was of the papular urticarial variety most commonly seen as the result of flea bites None was of the rarer bullous variety

In none of the excised specimens was there any significant change in the epidermis Most of the abnormal observations were in the subpapillary and deeper portions of the corium (fig 5) These consisted

17 Hartman, M The Use of Hormones in Dermatology, Brit J Dermat. **60** 30 (Jan) 1948

18 Hutchinson, J , cited by MacKenna, R W Diseases of the Skin, ed 3, Baltimore, William Wood & Company, 1933, p 278

19 MacKenna [18]

SUMMARY

The clinical characteristics of hereditary anhidrotic ectodermal dysplasia are described, emphasis being placed on the diagnostic triad of symptoms anhidrosis, hypodontia and hypotrichosis The most important dermatopathologic abnormality, complete or almost complete lack of formation of sweat glands, is pointed out, along with its effect on the patient's heat-regulating mechanism The several modes of hereditary transmission of the syndrome, as well as the embryologic development of the anomalies, are discussed The essential similarities and differences between the anhidrotic syndrome and hidrotic ectodermal dysplasia, Werner's syndrome, Rothmund's syndrome and the Hutchinson-Guilford type of progeria are pointed out in tabular form Four patients who were affected by the anhidrotic syndrome, 2 of them infants, are reported on in detail The report includes physiologic investigations of sweating, histopathologic examinations of epidermal tissue and inquiries regarding the genetic transmission of the anhidrotic syndrome in each patient's family group There is need that the syndrome be recognized promptly, particularly in an infant, so that the child may not be exposed to a warm environment and, as his development progresses, may have the benefit of dental prostheses early enough to prevent some of the facial abnormality which results from uncorrected hypodontia or anodontia

in a lymphocytic infiltration around the blood vessels, which were dilated and often filled with the lymphocytes The same lymphocytic infiltration occurred around the sweat and sebaceous glands and, in 1 case, around the muscle fibers In three of the specimens there was a very pronounced lymphocytic infiltrate around the sweat glands deep in the corium and even as deep as into the fat layer (fig 6) I was impressed by the intensity of this deep lymphocytic reaction

DATA OBTAINED FROM OUR LETTERS OF INQUIRY

In the fall of 1947 my associates and I mailed letters to all certified dermatologists in the United States, Canada, Hawaii and Cuba, asking about the flea problem in their communities

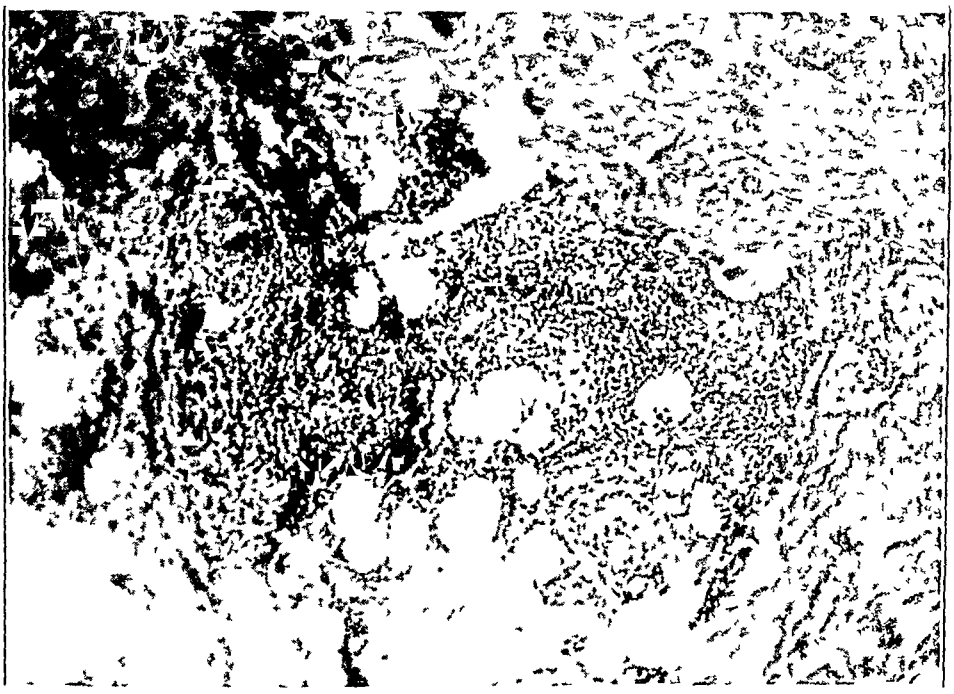


Fig 6—Histologic changes seen in the flea bite Note the intensity and the depth of involvement in the fat layer

The data in the letters received showed that fleas are a major dermatologic problem only in California Of the several hundred answers from all other parts of the country only a few persons gave as their opinion that fleas were a major medical problem in their community A slightly larger, but still small, percentage of letters stated that fleas were a minor problem In two states, Nevada and Colorado, some observers denied that cat and dog fleas even existed there

In California, however, in all letters from the San Francisco Bay area there was agreement that a real problem exists In eight letters from Los Angeles four dermatologists stated that the problem exists and four denied it All six letters from the Los Angeles suburbs contained statements that a moderate problem exists From the San Diego

FLEA PROBLEM IN CALIFORNIA

C J LUNSFORD, M D
OAKLAND, CALIF

THE TESTIMONY of present day dermatologists is that fleas are more of a nuisance in California, particularly in the San Francisco Bay area, than elsewhere in the United States

HISTORICAL ACCOUNTS

In the vast literature relating to exploration, settlement and life in California the references to misery caused by fleas encountered by the authors are related entirely to experiences in Northern California

Padre Juan Crespi,[1] the diarist of the Portola expedition of 1769, wrote that when the expedition visited an Indian village on Purisima Creek in San Mateo County they found the grass huts so infested with fleas that they called it "Village of the Fleas"

In 1786 the Frenchman La Perouse [1] had this to say about the fleas in Carmel and Monterey "Under the influence of the Missionaries the Indians had refused to make the slightest change in the construction of their huts because they could set fire to their huts when the fleas became a pest and could rebuild them in two hours"

Another Frenchman, Duhart-Lilly (1827-1828) [1] visited a ranch in the San Bruno Valley Concerning the sleeping arrangements he wrote, "We were compelled to stow ourselves away, guests, husband, wife and children all together, upon a great feather bed, where devoured by fleas we passed quite an uncomfortable night"

In the period of transition from Mexican sovereignty to that of the United States, the American Edwin Bryant, in his outstanding book, "What I saw in California," [1] wrote bitterly and in detail of the infestation of the rancheros and old missions with fleas He spoke of the missions as "nurseries of fleas" "If any sinning soul ever suffered the punishment of purgatory these torments were endured by myself last night," he said After a sleepless night there was no square inch of his body that was free from flea bites

Read at the Sixty-Eighth Annual Meeting of the American Dermatological Association, Inc, San Diego, Calif, April 28, 1948

1 The Flea in California History and Literature, California Hist Soc Quart **15** 329 (Dec) 1936

area 80 per cent of the letters had claims that fleas are a real problem Writers from Pasadena, Santa Barbara, Fresno and San Jose disclaimed that there is a flea problem in their localities

The writers described about the same varieties of eruptions as I have described A few specifically mentioned papular urticaria in children

Flea Antigen The great majority of the men stated they had had no experience with the use of flea antigen Most of those who had used it were from California, and their opinions varied from those of its being worthless to others that it was satisfactory in 70 to 80 per cent of cases treated Several men observed that the results were highly successful in some cases and that treatment completely failed in others

Results Reported from the Use of Locally Applied Repellents—The best results reported from the use of locally applied repellents and insecticides were obtained by those persons who used 0 5 to 10 per cent DDT (2,2-bis[*p*-chlorophenyl] 1,1,1-trichloroethane) Many military observers felt that Army 612 (2-ethyl-hexanediol-1,3) is, on the whole satisfactory Others reported varying results from the use of pyrethrum, rotenone and sulfur powder

Reports on the Use of Thiamine Hydrochloride Many of the men had used thiamine hydrochloride given by mouth as a repellent with varied results Eder [20] reported good results in both prevention and treatment Two reports from San Francisco had observations that thiamine hydrochloride administered internally was a 100 per cent effective repellent of fleas in human beings, cats and dogs According to others, it was of questionable value or completely worthless

Selectivity of Fleas Several of the men called attention to the selectivity of the action of fleas That is, very often in a family fleas will bite one member and not another, children being the most frequent victims Those in our office agree that this observation is an accurate one

Some of the men were attacked by human fleas but not by fleas from their own dogs Several observers were attacked by fleas in one geographic location but not in another For instance, fleas in their place of residence in San Francisco did not annoy them, but when they visited Los Angeles or some foreign city, such as Mexico City or Vienna, they would be severely bitten, the reaction in these cases being described as a severe bullous eruption

Some of the men thought that such things as body odor and sex hormones should be considered as accounting for the age and sex selectivity

20 Eder, H L Flea Bites Prevention and Treatment with Thiamin Chloride, Arch Pediat **62** 300 (July) 1945

The Rev Walter Calton (1850), in his book "Three Years in California,"[2] described the continued annoyance caused by fleas to strangers and observed that the native was not troubled by them

Carl Meyer (1855), under the title "Nach dem Sacramento,"[1] described a night spent on a ranch near Salinas He labeled his experience "flea fever"

> Hardly has one gone to bed when a band of these small devilish fleas pursue their bloody maneuvers on one's sensitive skin, driving away sleep and tormenting a man to madness One breaks out in a torturing sweat, and because of the frequent throwing off of the covers one runs a risk of contracting a fever

He mentioned that even in mixed company the subject of fleas was often the topic of conversation and that the gesture of scratching was not frowned on

Ernest de Massey wrote in his "Frenchman in the Gold Rush"[1] of his experiences in San Francisco

> There were millions of fleas in the sand near my shack On the floor was a layer of sand, the camping ground of a colony of fleas, which hopped around looking for a chance to make a good meal off me [and] by the time I was ready to retire my legs were literally covered with these blood thirsty insects

Frank Marryat, an Englishman, in his "Mountains and Molehills"[1] described his experiences in Santa Rosa, Calif On being shown his quarters he was "immediately attacked by the fleas with a vigor which was perfectly astonishing" He had been a wide traveler and had "been tortured by sand fleas in the Eastern Archipelago and by all kinds of mosquitoes from Malta to Acapulco," including the "famous 'tiger' breed against which there is no recourse but flight" "But," he said, "I would have preferred any of those annoyances to the attack of those Santa Rosa fleas" "The place was alive with them and they, raised in the rough school of the wild bullocks' hide, boldly faced as they attacked us" He stated that, on his mentioning the fact, his host predicted that he would get used to the fleas that he [the host] and his family never gave them a thought Thus the early settlers in California had observed that one became immunized against the effect of flea bites by being bitten by the fleas

In the San Francisco *Argonaut* of Dec 8, 1878,[1] there appeared a humorous article with the title "The Flea A Short Discourse on a Lively Subject" The author gave an account of his experiences with fleas encountered near what is now Redwood City At that time it was believed that fleas lived in the soil The author chose a site for his

2 Calton, W Three Years in California, New York, A S Barnes & Co, 1850, p 70

COMMENTS AND STUDIES ON IMMUNOLOGY

The entomologists say that the old idea of host specificity is erroneous Persons who think they are not bitten by fleas from their own dogs actually may have been bitten until they have established an immunity Also, some persons not bothered by fleas at home may be sensitive to a slight variation in antigen from fleas in a strange city

It appears that as a person continues to be bitten he undergoes a natural desensitization to the antigen deposited by the flea This takes place gradually over a period of about a year There are people, however, in whom this desensitization occurs more slowly, and in some cases it never occurs Patients have been known to leave the Bay region permanently because the fleas have made their lives intolerable

The biologic explanation for the phenomenon of natural desensitization against insects is illustrated by an experiment done by Kenneth Mellanby [21] To study the varying reactions to insect bites in man he fed the yellow fever mosquito on Englishmen who had never been away from the British Isles The first bites produced an erythema about 1 to 2 mm in diameter and in twenty-four to forty-eight hours a delayed reaction consisting of an intensely pruritic urticaria-like papule 1 cm in diameter surrounded by a 2 to 3 cm zone of redness After the subjects had been bitten for a month the immediate reaction was an itching wheal which was followed by the delayed reaction in twenty-four to forty-eight hours The later reaction recurred each three to four days As the experiment continued the delayed reaction gradually disappeared and there was less itching, but the immediate reaction never failed to appear Dr Mellanby stated, however, that many Englishmen bitten by thousands of indigenous mosquitoes finally lost the immediate reaction and had complete desensitization He expressed the opinion that the two reactions were quite distinct and were caused by different antigens in the saliva of the mosquito

My associates and I believe our clinical observations tend to show that a similar process of desensitization occurs naturally on prolonged exposure to flea bites

In 1939 Cherney, Wheeler and Reed [22] tested two groups of persons to an antigen made from dog, cat and human fleas indigenous to San Francisco About 85 per cent of the immune group gave no reactions A number of susceptible persons were given weekly injections for six weeks with the flea antigen in an attempt at desensitization The results of treatment were fair

21 Mellanby, K Man's Reaction to Mosquito Bites, Nature, London **158** 554 (Oct 19) 1946

22 Cherney, L S , Wheeler, C M , and Reed, A C Flea-Antigen in Prevention of Flea Bites, Am J Trop Med **19** 327 (July) 1939

home near a ranch called "Rancho de las Pulgas," where the beauty of the country impressed him He observed that potatoes planted in the soil had to be removed with a crowbar because of the hardness of the soil and that the potatoes when dug were as "flat as pancakes" He thought that fleas could not live in such soil On calling on the owner of the ranch he noticed a stick ladder leading from the floor to a high attic under the roof, where the household slept The significance of such an arrangement became apparent when, on being severely bitten about his ankles, he looked down and saw that his white socks were covered with "pepper in motion" The home owner then told him that his routine for sleep was to remove all his clothes, leave them on the floor and scurry up the ladder, leaving only the clothes for food for the fleas Subsequently the author learned that "Rancho de las Pulgas" signified "The Farm of the Fleas"

ENTOMOLOGY OF FLEAS [3]

The three species of fleas most commonly attacking man in the United States are the human flea (Pulex irritans), the cat flea (Ctenocephalides felis) and the dog flea (Ctenocephalides canis) In the eastern part of the United States the dog flea is the dominant pest In the South and West the human flea is In California the human flea and the cat flea are equally dominant (fig 1)

The eggs of all these species hatch in the nests or resting places of their hosts, rarely on their bodies, or else in dust or organic debris in buildings Following the life cycle of any insect, from egg to larva to pupa within the cocoon, the adult flea emerges in about two weeks Newly emerged adults are usually very fat and can live for several months, under favorable conditions, without feeding The female flea must have a blood meal before her eggs can be fertilized Most fleas visit the body of the host for relatively short periods for the purpose of obtaining a blood meal

On smooth surfaces, fleas progress by means of short jumps They may sham death when disturbed They usually leave a dead host as soon as the body becomes cold They like warmth and moisture but shun daylight It has been determined that some adult fleas can jump vertically nearly 8 inches (20 cm) and horizontally 13 inches (33 cm) Fleas prefer hosts with nests

The life cycles of fleas are decidedly influenced by meteorologic factors Low atmospheric humidities in particular are inimical to them

3 The data and some of the phrasing on entomology were given to me by Morris A Stewart, Ph D , Professor of Parasitology, the Division of Entomology and Parasitology, University of California, Berkeley, Calif

In 1941 McIvor and Cherney [23] treated persons sensitive to flea bites by injecting into them an antigen extracted from whole San Francisco fleas They reported encouraging results

On the basis of data shown in McIvor and Cherney's article the Lilly Research Laboratory prepared an antigen according to the methods developed by the authors but obtained dog, cat and human fleas from Bolivia and Mexico City This extract has been used in our office since it was first manufactured in the treatment of children who were most persistently susceptible to flea bites The results obtained were not controlled and were difficult to evaluate properly because we could not determine whether the "cure" was the result of the injections or was an expression of a natural immunity developed from the patient's being constantly bitten by fleas

Hatoff,[24] using Lilly's commercial antigen and a technic similar to that used by McIvor and Cherney,[23] reported successful desensitization in about four fifths (80 per cent) of children treated

We feel that studies should be made to determine whether or not there is a difference in the antigen injected by fleas of different kinds and from different localities and, if so, of what clinical importance it is

EXPERIMENTS WITH FLEA ANTIGEN

With the cooperation of Drs Bernard H Winston of Kansas City, Mo, and Knox Freytag at the Presidio in San Francisco, together with the residents at Highland–Alameda County Hospital in Oakland, 45 children and 104 adults were tested with the Lilly flea antigen, the tuberculin technic being used Results are so lacking in uniformity that no conclusions can be drawn Therefore, we wish to reserve our findings until they have been rechecked

STUDY OF REACTIONS TO FLEA BITES

It is difficult for one to obtain fleas because of the present day universal use and efficiency of DDT as an exterminator The fleas we have used have been cat fleas, obtained from dogs [25] These fleas were fed on the forearms of volunteers The hungry fleas fed without hesitation When the fleas were satisfied they became active We usually used six to twelve fleas on each subject At times we could get only three or four The fleas will feed three or four times a day and can be kept alive in the test tube with such feedings on the average of only ten to fourteen days

23 McIvor, B C, and Cherney, L S Studies in Insect Bite Desensitization, Am J Trop Med **21** 493 (May) 1941

24 Hatoff, A Desensitization to Insect Bites, J A M A **130** 850 (March 30) 1946

25 The fleas used in our experiments were furnished through the courtesy of Morris A Stewart, Ph D

The length of time required for each developmental stage is very largely determined by the prevailing temperature and humidity Adult fleas may remain alive for more than five years if the environmental conditions are favorable, such extremely long adult life is, of course, very exceptional, usually the flea lives only a few weeks or months Because of the lack of extremes in temperature and the relatively high humidity, in coastal California fleas breed the year around They are found in homes where cats and dogs are kept as pets, particularly in the carpets and cracks of floors and corners of rooms They are found in basements where the animals sleep at night They are particularly apt to be found in large numbers in such basements from which the usual animal



Fig 1—Cat flea (Courtesy of Morris A Stewart, Ph D, Department of Entomology, University of California, Berkeley, Calif)

and human tenants have been absent for a period I know of persons who have walked into their own basements after a summer vacation, to have their white trousers literally covered with very hungry fleas in a few seconds Fleas also frequent outhouses, sand piles and lawns and such places as theaters I know of people who are bitten by fleas whenever they attend any theater

CLINICAL PICTURE

The typical clinical picture of reaction to flea bites is a grouped, itching, urticarial, papular eruption, some papules of which contain a central red punctum (fig 2) These lesions are most often found along the

EXPERIMENTS

With Normal Conditions—EXPERIMENT 1 The fleas were fed on 12 members of our office staff and their families All except 1 were old residents of the Bay region The exception had been reared on a ranch and knew that she had been exposed to fleas all her life Although the fleas fed with equal avidity on all 12 subjects, only 2 persons showed a positive reaction Both of these had been flea-sensitive all their lives The reactions were both immediate and delayed This experiment demonstrates the immunity of 10 out of 12 old time Californians to flea bites

EXPERIMENT 2—Fleas were fed on 8 volunteer students at the University of California in Berkeley, none of whom gave a history of previous sensitivity to fleas Of the 7 that returned for observation only 1 had been a resident of the San Francisco Bay region for longer than two months The exception had lived here for six months Seven of the 8 volunteers showed a positive delayed reaction at the end of forty-eight hours This experiment indicates the sensitivity of recent residents in the Bay region to flea bites

EXPERIMENT 3—Fleas were fed on 4 bottle-fed newborn babies at the Highland-Alameda County Hospital None of the babies had been out of the hospital At the end of forty-eight hours there had been no reaction This experiment indicates that persons on first being bitten by fleas are not sensitive to their bites

With Local Application of Repellents—Oil of Citronella Two of our nurses applied oil of citronella to their forearms The fleas were repelled and did not feed It was interesting to see them dance all over the feeding ground

Pyrethrum Two subjects had powder containing 0 7 per cent pyrethrum dusted on their forearms In 1 case the fleas fed In the other the fleas were repelled after five minutes of feeding In both instances fleas were listless for twenty-four hours and would not feed but recovered In 2 other subjects other fleas were exposed to a heavier powder sprinkling Although we did not see them feed, they all died in twenty-four hours

Army 612 (2-ethyl-hexanediol-1, 3) Three subjects were tested The fleas were repelled, and most died within twenty-four hours

DDT Powder (7 5 per cent DDT) Two subjects were studied The fleas would not feed after five minutes and died in four hours We did not pursue this experiment because we could not afford to kill more of the fleas

Camphor Spirits of camphor was applied to the forearms of 6 subjects, and fleas were placed thereon The fleas would not feed One volunteer forgot to cleanse the camphor from his forearm properly Four hours later two tubes of fleas were fed on the same site The fleas were dead in fifteen minutes

Petrolatum In four instances fleas would not feed through petrolatum rubbed on the forearm

With Internally Administered Repellents—Sulfur Four patients were fed calcium sulfide, ¼ gram (15 mg) twice a day for seven days Fleas fed normally and were not made ill We have been advised that farmers in certain parts of the country, believing that sulfur will protect them from fleas, take it in the spring for that purpose

Quinine Eight tubes of fleas were fed on 4 subjects given 5 grains (0 30 Gm) of quinine sulfate three times a day for three days At the end of thirty-six hours 90 per cent of the fleas were dead

Thiamine Hydrochloride One subject was given 100 mg of thiamine hydrochloride, intramuscularly One half hour later the fleas fed Six hours, ten hours

waist line and on the hips and shoulder area, where the clothing fits snugly (fig 3) They may, however, be on any part of the body Grouping is one of the most characteristic features The flea is not content to bite in one area and remain attached at that point until its hunger is satisfied Rather, it moves along, biting in an irregular but grouped

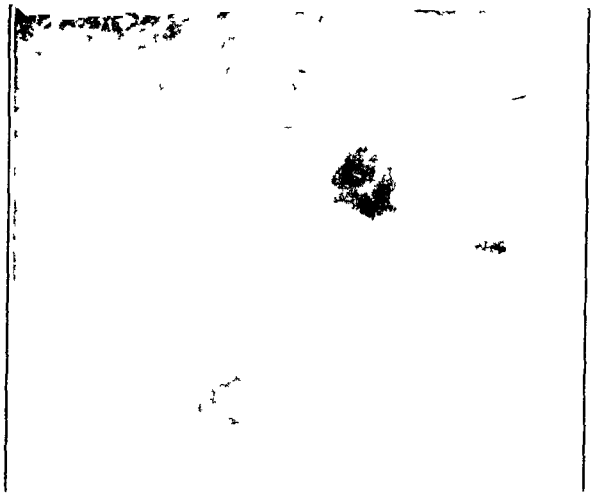


Fig 2—Individual flea bites, showing papules, central puncta and vesiculation



Fig 3—Flea bites in typical round the waist distribution (Courtesy of Rees B Rees, M D, San Francisco)

pattern In addition, there may be more scattered or satellite lesions present In some cases a generalized papular urticaria is seen (fig 4) It is believed that many of such papules are allergic reactions to one or a few bites and are an expression of sensitivity to the antigen injected

and twenty-two hours later, fleas were repelled and would not feed on either the subject or 4 other subjects who had not taken thiamine hydrochloride Two days later the fleas fed on the original subject

Four subjects were given 100 mg of the drug intramuscularly at 11 a m, 4 30 p m and 10 30 a m the next day At 1 p m fleas were planted on all subjects and fed for five minutes, and then they quit feeding At 8 a m, 9 a m and 3 p m the next day the fleas would not feed At 8 30 a m the third day most of the fleas were dead The fleas that remained alive fed

Seven test tubes of fleas were fed on 3 subjects given 100 mg of thiamine hydrochloride by mouth, three times a day At the end of six hours the fleas fed reluctantly At subsequent plantings they fed for only five minutes and were inactive At the end of three days most of them were dead

This experiment indicates that at first fleas are repelled but later feed and die when they are planted on patients given thiamine hydrochloride

Fleas were fed on 4 persons with a history of sensitivity to fleas There developed a typical flea bite reaction After the subjects had taken three doses of 100 mg of thiamine hydrochloride, the fleas were again fed on them The subsequent effect was either a less severe reaction or none at all

The question arises as to whether this lowered reactivity was due to the desensitizing or to the repellent action of thiamine hydrochloride

CONTROL OF FLEAS

The most practical method of controlling the flea problem is by means of the newer insecticides, such as DDT If this substance is sprayed onto carpets, floors, overstuffed chairs and basements the fleas will be quickly destroyed It is not necessary for one to apply it to dogs and cats to rid them of fleas Instead it should be sprayed into their kennels or nests or onto their favorite sleeping places One such spraying every two months will keep animals free from fleas

CONCLUSIONS

Flea bites constitute an annoying problem in coastal California, particularly to newcomers in the San Francisco Bay area

My associates' and my experiment of feeding fleas on newborn infants confirms our clinical observations that persons first have to be bitten by fleas in order to become sensitive Our experiments of feeding fleas on old time Californians and on newcomers confirm our clinical findings that most people become immune after having been bitten over long periods

We are certain that most cases of "papular urticaria" in California are, in reality, due to flea bites and suspect that this is probably true elsewhere

Further studies and better antigens are needed for the investigation of the value of artificial desensitization

Oil of citronella, pyrethrum, Army 612, DDT, petrolatum and camphor applied locally are of value as repellents

her closely but could get no history of the ingestion of arsenic I simply think that we have to decide whether this entire picture should be included in a single dermatologic entity, which I rather doubt at present

DR HAMILTON MONTGOMERY, Rochester, Minn I thought this was a case of congenital defect She has a flat nose You could not call it a congenital ectodermal defect with the changes in the tongue, but we have seen cases of endodermal and ectodermal changes merging together She did not have changes in the teeth but had changes in the palms that might indicate an ectodermal defect, as would the changes in the neck In addition she has apparently had a dermatitis which does not belong with that picture I would suggest that her family history be investigated

DR FRANCIS W LYNCH, St Paul, Minn I thought of the possibility of an ectodermal defect, but the mucosal changes were too great The family history is normal as far as could be learned on brief questioning

Darier's Disease (Keratosis Follicularis), Improvement Following Vitamin A Therapy Presented by DR S J ZAKON and (by invitation) DR A L GOLDBERG

A Case of Keratosis Follicularis with Cutaneous, Mucous Membrane and Nail Changes Presented by DR CLEVELAND J WHITE and (by invitation) DR ROBERT H HARRIS

A Case for Diagnosis (Drug Eruption? Neurotic Excoriations? Cutaneous Tuberculosis?) Presented by DR D V OMENS and (by invitation) DR H D OMENS and DR J GRAFFIN

A Case for Diagnosis (Sarcoidosis?) Presented by DR M H EBERT and (by invitation) DR ALLEN PEARL

Sarcoidosis Presented by DR STEPHEN ROTHMAN and (by invitation) DR EDWARD LADEN

Multiple Neurofibromatosis of Von Recklinghausen Presented by DR THEODORE CORNBLEET and (by invitation) DR D COHEN and DR J GRAFFIN

Multiple Neurofibromatosis Presented by DR EDWARD A OLIVER and staff of Hines Hospital

Rupial Syphilid Presented by DR D V OMENS and (by invitation) DR HAROLD D OMENS and DR N L BAKER

Secondary Syphilis and Granuloma Inguinale (?) Presented by DR JAMES R WEBSTER and DR S M BLUEFARB and (by invitation) DR N L BAKER.

Chronic Urticaria Due to Intestinal Organisms, "Giardia Lamblia", "Cure" Following Treatment with Quinacrine Hydrochloride Presented by DR JAMES H MITCHELL and (by invitation) DR ROBERT H HARRIS

Folliculitis Decalvans (?) Presented by DR JAMES H MITCHELL and DR ROBERT H HARRIS (by invitation)

Folliculitis Decalvans Presented by DR F E SENEAR and staff

A Case for Diagnosis (Leprosy?) Presented by DR F E SENEAR

Linear Lichen Planus Presented by DR JAMES H MITCHELL and DR RALPH SCULL and (by invitation) DR BERNARD YAFFE

Epidermolysis Bullosa Presented by DR F E SENEAR and staff

Widespread Morphea with Acute Development Presented by DR STEPHEN ROTHMAN and (by invitation) DR LOUIS RUBIN

Two Cases for Diagnosis (Unrelated), (Lichen Sclerosis et Atrophicus?) Presented by DR THEODORE CORNBLEET

Eosinophilic Granuloma Presented by DR EDWARD A OLIVER and (by invitation) DR E LORANT

Pityriasis Rubra Pilaris Presented by DR S ROTHMAN and (by invitation) DR J H MCCREARY

Eczema Vaccinatum Presented by DR F E SENEAR and staff

A Case for Diagnosis (Secondary Vaccinia [Autoinoculation]) Presented by DR F E SENEAR and staff

The continued taking of quinine by mouth or of thiamine hydrochloride by mouth or injection is of clinical and experimental value in the repelling of fleas

Modern insecticides, such as DDT, applied to the known breeding places of fleas offer the most practical solution of the problem

3115 Webster Street (9)

ABSTRACT OF DISCUSSION

DR LESLIE M SMITH, El Paso, Texas I spent the summer of 1925 in the clinic of Dr Harry Alderson at Stanford, and I have had both clinical and personal experience with the hardy California fleas I have seen reactions to their bite so severe and extensive as to suggest erythema multiforme or urticaria That allergy to the toxins injected by fleas and other insects occurs in some persons there can be little doubt This is evidenced by the extreme local reactions which occur in some victims and, I believe, by the appearance of some urticarial lesions which do not occur at the sites of bites, or at least do not contain the puncta of typical bites

In the El Paso area, on account of the very low humidity, fleas are no problem There are mites, bedbugs, mosquitoes and some other insects, and manifestations of allergy are occasionally observed following the bites of some of these In addition to typical bites one occasionally sees scattered urticaria papules, which do not appear to be the result of bites and presumably are an allergic response to absorption of toxin from the bitten areas

I am not prepared to state that in patients encountered in my practice insect bites are the principal cause of lichen-urticatus-like eruptions, but I think it is quite probable that I have not been sufficiently alert to the possibility of this factor in such cases It is a common observation that most cases of lichen urticatus and prurigo occur among the type of patients in whom malnutrition is common These same patients usually live under conditions which favor the presence of insects and the possibility of insect bites I, for one, shall be more conscious hereafter of the possible role of insects in the lichenoid and urticarial papular eruptions

I have had no experience with treatment by desensitization to insect toxins, but the fact that a person may gain tolerance after being repeatedly bitten would seem to indicate that tolerance might be produced artificially by hypodermic injections of the proper antigen I believe this line of reasoning is worthy of further work

In areas where fleas constitute such a problem as they do in California, it is probably wise to give orally or parenterally administered repellents, such as quinine or thiamine, to susceptible persons, but where fleas and other insects are not so numerous I believe the intelligent use of repellent sprays about their breeding places and about the patient's environment will be sufficient for their control

I should like to know what success Dr Lunsford has had with use of the antihistaminic drugs in the control of reactions to insect bites

DR PAUL E BECHET, Elizabeth, N J Dr Lunsford's paper is of interest, in view of the fact that plague-infected fleas (Xenopsylla cheopis) caused the unprecedented death of over 60,000,000 persons from the year 1348 to the end of the Seventeenth Century Another killer of men, typhus, can be carried by fleas as well as by lice, which observation calls attention to the fact that Hieronymus Fracastorius, the author of "Syphilis sive Morbus Gallicus" published "Contagion,

lusterless, pierced the crusts and scutula There was an offensive "mouse" odor to the scalp There were numerous areas of atrophic scarring with alopecia Examination by means of the Wood filter revealed a dull gray fluorescence of about 60 per cent of the hairs of the scalp Of interest was the fact that the involved hairs were fluorescent throughout their length Several of these hairs were pulled for microscopic examination The hairs pulled with some difficulty, though with no pain to the patient Exerting tension on the hair gave one the same impression as pulling a stiff rubber band, i e, the hairs were distinctly tensile

Two finger nails were involved slightly, the process beginning at the distal lateral portion of the nail Microscopic examination of the nail from these areas showed numerous myceliums

Microscopic examination of hairs treated with a 20 per cent solution of potassium hydroxide revealed large spores, many in long chains and others occurring individually In crusts clinging to hairs, hyphae were extremely numerous The spores were seen within the entire length of the hair shaft Also noted within the shaft were numerous air bubbles

A tentative diagnosis of favus was made, and material was sent to Dr E D DeLameter of the Mayo Clinic and to Mr David Mitzkus of the Mycology Laboratory at the Army Area Laboratory, Fort Sam Houston, Texas, for culture Both laboratories reported growth of Achorion schoenleini

The patient has refused roentgen epilation, and treatment has consisted of manual epilation, with the use of a General Electric Purple X® bulb for fluorescence and topical application of an ointment of 20 per cent zinc undecylenate with 5 per cent undecylenic acid (zincundecate [desenex®]) and other fungicidal preparations Most of the improvement noted is apparently due to the correction of the hygienic status of the scalp At this time the infection is still unchecked

A questionnaire was sent to several dermatologists throughout the state Dr Bedford Shelmire of Dallas stated that he had seen 2 cases of favus, which apparently were endemic, within the past twenty years Dr C F Lehmann and Dr J L Pipkin of San Antonio, reported that "the only cases of favus which we have seen were outside San Antonio" All others questioned stated that they had never seen a case of favus in Texas

112 West Seventh St

CONGENITAL DERMOID INCLUSION CYST

Report of a Case

MAURICE J COSTELLO, M D
NEW YORK
WILLIAM F LOVEBURY, M D
COLUMBUS, OHIO
AND
JOHN F DALY, M D
NEW YORK

Dermoid cysts situated on the bridge of the nose are relatively rare, and while seen occasionally by otolaryngologists they have not been brought to the attention of dermatologists

This type of cyst belongs to the group of tumors found about the nose which, according to Luongo,[1] result from the trapping of a portion of the dermis by

1 Luongo, R A Dermoid Cyst of the Nasal Dorsum Arch Otolaryng **17** 755-759 (June) 1933

Contagious Diseases and Their Treatment" in 1546, and in his discussion of the etiology of typhus stated that it is caused by a "germinis" transmitted to man by the bite of an insect and not by direct contact or fomites This brilliant observation of Fracastor's four centuries ago was unfortunately completely ignored, had it been acted on and further investigated, it would have saved millions of lives

I hope I may be pardoned for bringing up the lethal importance of the flea, rather than its dermatologic significance, and also that Dr Lunsford may not suffer for his temerity by mentioning fleas and California in the same breath

DR N P ANDERSON, Los Angeles When I first came to California I mistakenly diagnosed flea bites as ordinary urticaria Occasionally the diagnosis of flea bites is made on the findings of bullous lesions the size of a walnut It is hard to conceive that such bullae can be the results of flea bites I think that Dr Lunsford, having access to so many fleas, could disprove the idea that a great many of these lesions are allergic It seems to me that this should be proved or disproved Take these fleas, isolate the person, and let one flea bite him to see whether lesions remote from the bite do occur I don't believe that these so-called remote lesions are allergic I have seen five hundred lesions on one member of my family At certain times of the year there is an epidemic of flea bites Such an epidemic is usually associated with hot spells Endemic cases are seen throughout the year I should also like to mention the transmission of disease by biting insects The bubonic plague first appeared in this country in the Chinese quarter of San Francisco early in the 1900's Oriental fleas carrying the transmittal agent of bubonic plague have been found as far east as Colorado This reservoir of plague extends over the nation and sometime in the future may burst forth into an epidemic

DR NORMAN EPSTEIN, San Francisco I had the pleasure of reading Dr Lunsford's paper at home, and I think he should be complimented on the well planned investigation which he has made Examination of the literature shows a lack of papers on this subject Those of us who practice dermatology in the San Francisco Bay area will concur in the conclusions which Dr Lunsford has drawn There may be some difference of opinion about certain points Dr Anderson has emphasized the role of the flea in transmitting diseases We are all familiar with that Some of us do not realize that bubonic plague, which is transmitted by the flea, still exists in this country There have been 506 cases of bubonic plague in America since 1900 There have been 300 reported from San Francisco, in 268 of which the patient died The last case was reported in 1942, but we cannot be assured that new cases will not develop when least expected Tularemia is spreading from California throughout the country and into Canada by way of fleas transmitted from one rodent to another I agree that a large majority of the cases of papular urticaria in San Francisco are very likely due to flea bites At times the eruption is so severe that some people have to move from San Francisco One of the most remarkable things about the flea is that it will not bite everyone This selectivity on the part of the parasite can hardly be explained on desensitization alone The work of Shannon in regard to thiamine hydrochloride in the repelling of mosquitoes may have a practical bearing in making certain parts of the world more habitable This work was done in 1933 Eder noted that fleas were repelled from children given thiamine hydrochloride Shannon expressed the belief that this action was due to a change in body odor of the person taking the thiamine hydrochloride Perhaps that is the explanation Usually one sees fleas on logs and flea bites on patients who work in warehouses on wooden floors The lesions are occasionally bullous

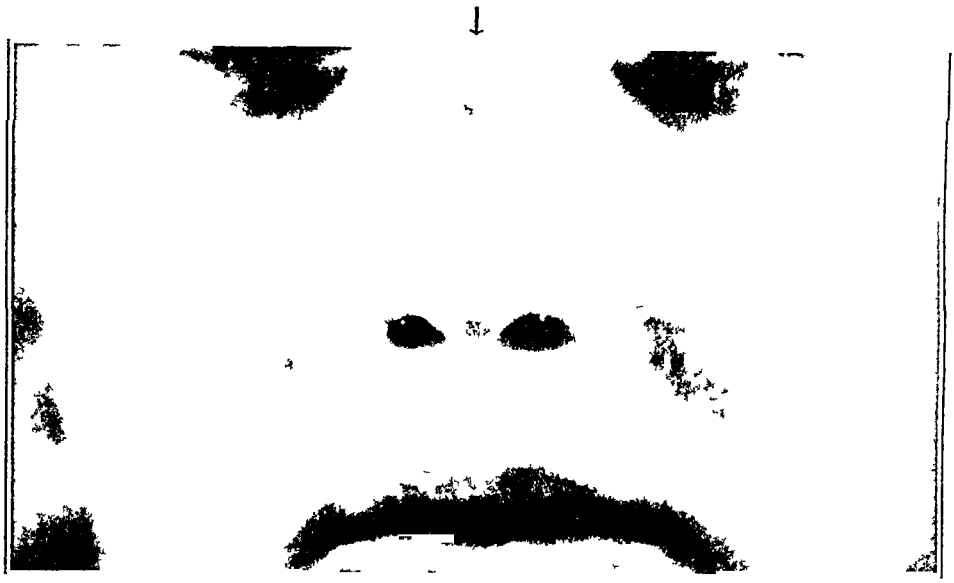


Fig 1—Congenital dermoid inclusion cyst of the nose, with protruding short, black hairs

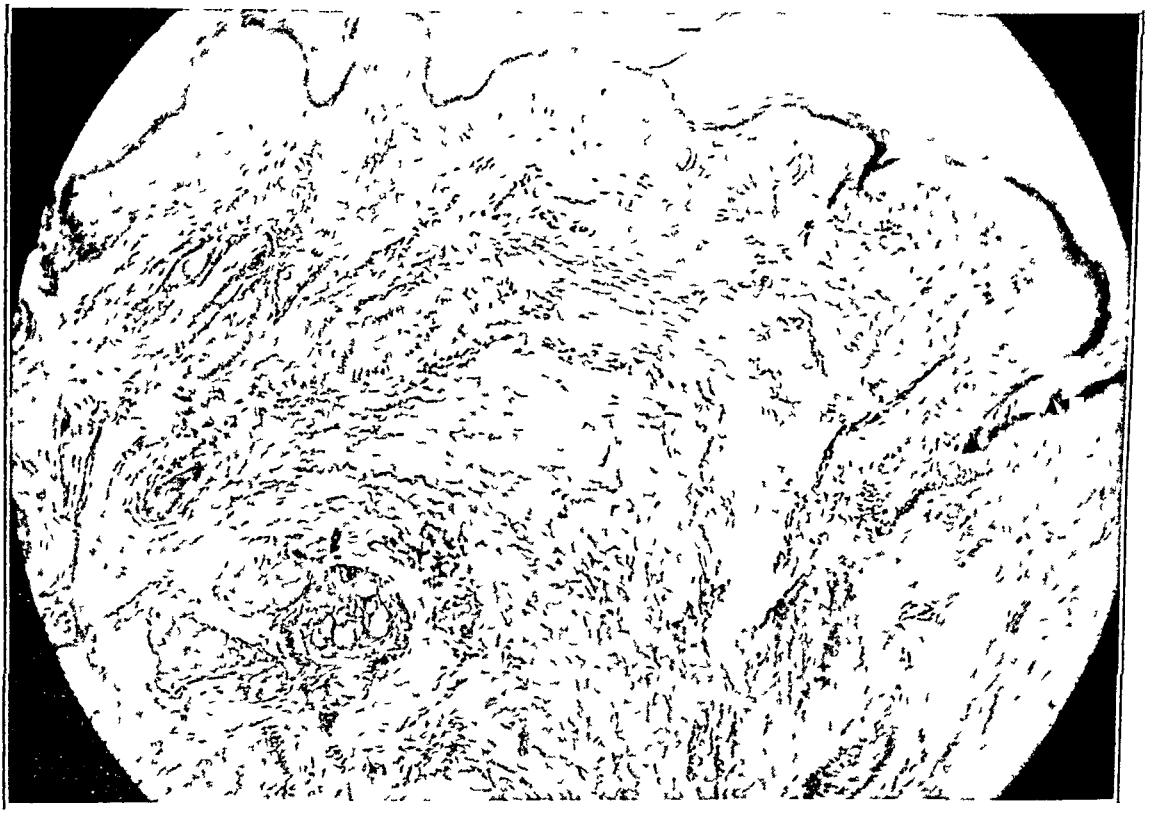


Fig 2—Partial view of the epidermis lining the floor of the cyst, low power magnification, hematoxylin and eosin stain

In our hands, the use of flea antigen has not been convincing in its effects My associates and I have been unable to say that flea antigen has accomplished very much clinically In our hands, the antihistaminic drugs have given some relief

DR. SAMUEL AYRES JR, Los Angeles With reference to humidity, it seems that in our part of the state the flea season is in the hot, dry months, beginning with July, August and September, when the humidity is low The definite instances of flea bites are more pronounced at this time The question of regional immunity is another interesting thing People reaching the Bay area become bitten, and I have also encountered long time residents of San Francisco who have been bitten by our variety of flea One can be immune to California fleas but not to Mexican fleas People may be bitten by cat and dog fleas in any part of the country I know of one person who has been susceptible to dog fleas and is unable to keep dogs Several years ago, in the literature, I ran across an account of an experiment in which a flea was put in the center of a round table and invariably hopped to one person regardless of his position at the table I have had some degree of success with the use of histamine azoprotein (hapamine®) desensitization for highly sensitive persons This drug did not stop the fleas from biting, but the reaction was much less severe An editorial in the *California Medicine* about eight months ago (Hartman, M M *Calif Med* **60** 242, 1947) mentioned the valuable effect of histamine azoprotein in treatment of insect bites Thiamine hydrochloride in a dose of 100 mg three times a day is of definite value in conferring temporary immunity

DR SAMUEL PECK, New York We have had relatively little experience with flea bites in New York city, but, if I may judge on analogy with the investigations which my associates and I carried out during the War ("Cutaneous Reaction Due to the Body Louse," *J A M A* **123** 821 [Nov 27] 1943), it is probable that the flea bite, like the louse bite, is an allergic reaction Pruritus became evident only after allergy was established

Interestingly enough, we could show that the feces as well as the bite of the louse played a role in the cutaneous eruptions which were produced

DR C F LEHMANN, San Antonio, Texas Since the question of allergy is brought up, I rise to testify that I have remained sensitized to the toxin of the flea bites since I was a small boy and was heavily infested with fleas while seeking shelter from a heavy rainstorm one night Ever since then, a flea bite will cause an urticarial reaction not only locally but also generally in me

The diagnosis of such bites sometimes presents quite a problem A child may be brought in with a line of papules with central puncta The flea has the propensity of crawling along a line and biting, and the line of papules is strong corroborative evidence of flea bites, despite the fact that the proud mother might not want to admit such things as fleas having bitten her child These lines of papules are sufficient evidence to substantiate the suspicion of the etiologic factor

DR H S ALDEN, Atlanta, Ga I don't believe that flea bites occur only in California We have them in Georgia In Georgia the "chigger flea" produces most of our troubles I should like to mention the fact that the Negro (the dark Negro, not the mulatto) is more or less immune to the bites of the chigger White men could not be worked in the swamps, but the Negroes could Once I tried to get some students to collect chiggers by laying a sheet or some white material on the ground The chiggers will come to that sheet in large quantities and can be collected I have therefore warned patients never to go into the woods with white shoes or white clothes

DR C J LUNSFORD, Oakland, Calif I thank all the discussers for their expressed interest in my paper

intrusion of the frontonasal plate between the embryonic nasal dermis and mucosa The bridge of the nose, exactly in the midline, is a common location

Most of these growths are discovered before the fifth year of age Secondary infection is common and is followed by sinus formation, with discharge of sebaceous material and pus Occasionally, as with the patient considered here, the presence of hairs calls attention to these congenital anomalies

REPORT OF CASE

A B, a white girl, was first seen by one of us (M J C) when she was 5 years old Her mother gave a history of noticing a small lesion on the bridge of the child's nose when she was 6 months old Since that time the growth had constantly had small black hairs and a thick discharge coming from the opening in the skin There was no family history of similar lesions or other congenital defects

Physical examination revealed a well nourished, well developed, white female child with no abnormalities except a small, match head–sized opening on the bridge of the nose at the junction of the cartilaginous and bony portions, exactly in the midline From this opening thirty to forty black hairs protruded The hairs were midway between lanugo and terminal adult hairs and could be removed easily with moderate traction On gentle pressure a thick, sebaceous material could be expressed There was little pain and no inflammatory reaction around the opening of the sinus

Treatment, which was carried out by Dr John F Daly, consisted in injecting methylene blue into the cyst to facilitate determination of the exact extent of the lesion An elliptical incision was made around the opening of the sinus, and the growth was completely dissected out It was found to mushroom out under the skin and was about pea sized, extending down to the junction of the cartilage and bone of the nose, but it did not involve either Grossly, the lining of the cyst looked like the skin of the scalp or bearded region

Histopathologic examination of the lining of the cyst revealed a normal-appearing epidermis except for a number of vacuolated cells in the basal layer The dermis contained no abnormal cellular elements but did show a large number of hair follicles with their associated sebaceous glands There was no evidence of sweat glands, a finding which has been consistent in previously reported cases

COMMENT

Congenital dermoid inclusion cysts of the bridge of the nose frequently extend down into the nasal septum and necessitate extensive surgery Other methods of therapy, such as electrolysis or destruction with high frequency current or cautery, often result in inadequate removal, recurrences and poor cosmetic results On one occasion, we saw a lesion such as the one described treated as a sebaceous cyst by electrosurgery with a final result of the development of a basal cell epithelioma

SUMMARY

A case of congenital dermoid inclusion cyst of the nasal dorsum is presented An excellent cosmetic result, with no recurrences of the growth, followed treatment

140 East Fifty-Fourth Street (22)

In answer to Dr Leslie Smith's question I have not had sufficient experience with the use of the antihistaminic drugs in the control of reactions to flea bites to permit me to discuss the subject

In answer to Dr Bechet's question as to the part blood-sucking insects play in producing the "cutaneous ills of mankind," my observations have in the main been limited to the bites of fleas In those cases in which the allergic reactions are expressed as generalized urticarial or erythema-multiforme-like eruptions, I think there is no doubt but that a rise in temperature would be present

Dr Anderson's idea of planting fleas on persons suspected of being allergic to flea bites and thus demonstrating whether or not such lesions as bullous ones develop far from the sites of the bites is an interesting one My associates and I hope to be able to follow through on it

I was interested in Dr Peck's experiment, proving that in the case of the louse the antigen producing the cutaneous reaction was obtained from the feces as well as from the salivary glands of the louse The group from the Hooper Institute, who did the original work in preparation of the antigen used by Eli Lilly, ground up the whole fleas, including the contents of the intestinal tract, in the production of their antigen In the case of fleas, however, the clinical observation of inflammatory reaction developing about the central punctum would make it appear likely that the flea antigen is in their salivary glands

We were interested to learn that Drs Epstein, Ayres and Lehmann agreed with us that fleas can produce an allergic response

LICHEN-SCROFULOSORUM-LIKE LESIONS ASSOCIATED WITH SARCOIDOSIS

Report of a Case

MATTHEW J BRUNNER, M D
AND
MILTON ROBIN, M D
CHICAGO

Lichen scrofulosorum is characteristically associated with a high degree of sensitivity to tuberculin, patients in up to 67 per cent of cases showing positive reactions to old tuberculin in a dilution of 1 1,000,000 [1] The finding of apparently typical lesions of lichen scrofulosorum in a patient exhibiting negative reactions to intracutaneous injections of old tuberculin in dilutions as low as 1 10 is therefore unusual Microscopic examination of cutaneous biopsy specimens in this case revealed a histologic structure characteristic of sarcoid, and on further study laboratory and clinical observations of sarcoidosis involving the eye, salivary glands and lungs were made The association of lichen scrofulosorum with sarcoidosis has been noted on several occasions in cases cited in the transactions of dermatologic society meetings, but the observation of a sarcoidal histologic pattern in lesions of lichen scrofulosorum is apparently unique Mitchell and Nomlund,[2] Cannon,[3] Cornbleet,[4] Michelson [5] and Becker [6] have reported on the clinical concomitance of the two conditions Biopsy of the lichenoid lesions in Cornbleet's case was reported as revealing hematogenous tuberculosis In Cannon's case, the histologic appearance was that of lichen spinulosus

REPORT OF CASE

A mulatto woman, aged 26, was seen in the Department of Dermatology, Research and Educational Hospitals, in August 1946, complaining of joint pains, dryness of the mouth, swelling of the glands of the neck and a cutaneous eruption of three months' duration There had been slight loss of weight, fatigability and low grade fever during this period Examination on admission to the hospital revealed a slender woman, apparently not acutely ill, with an eruption on the neck, shoulders and back, consisting of grouped, acuminate, pinpoint-sized to millet seed–sized, skin-colored papules, some of which were pierced by short, horny spines A few of the patches had cleared centrally to produce annular lesions (figure) There were numerous areas, from the size of a dime to that of a quarter,

From the Department of Dermatology, University of Illinois College of Medicine, Dr F E Senear, Director

1 Sulzberger, M B Dermatologic Allergy, Springfield, Ill, Charles C Thomas, Publisher, 1942, p 234

2 Mitchell, J H, and Nomlund, R Lichenoid Sarcoid and Lichen Scrofulosorum, Arch Dermat & Syph **35** 334 (Feb) 1937

3 Cannon, A B Lichen Scrofulosorum and Sarcoid, Arch Dermat & Syph **38** 91 (July) 1938

4 Cornbleet, T Tuberculosis Cutis (Scrofuloderma, Sarcoid and Lichen Scrofulosorum), Arch Dermat & Syph **38** 272 (Aug) 1938

5 Michelson, H E Sarcoidosis, Arch Dermat & Syph **46** 774 (Nov) 1942

6 Becker, S W Sarcoid (Miliary), Arch Dermat & Syph **48** 223 (Aug) 1943

Clinical Notes

PAIN IN A BREAST DUE TO NEUROSYPHILIS

CARL F BAUMEISTER, M D
RIVERSIDE, ILL
VICTOR P SLEPIKAS, M D
BERWYN, ILL
AND
DUANE D DARLING, M D
CHICAGO

ANY NEW manifestation of syphilis is a matter of clinical interest The literature fails to reveal an authenticated instance of neurosyphilis as a cause of pain in a breast

REPORT OF A CASE

Mrs K D, aged 55, had pain in the right breast, increasing in amount for five years This pain would tend to come in waves of sudden onset, severe intensity and varying duration of one to thirty minutes and would terminate with a feeling of soreness The number of attacks in twenty-four hours would vary, but they were tending to occur almost continuously in the month prior to her hospitalization, which occurred in February 1947 When the patient had an attack and was not taking opiates she could obtain relief only by squeezing her breast violently Since this was not very effectual, codeine or other opiates were given four or five times daily, with partial relief

Since the pain was equally severe and bizarre, the patient had seen numerous physicians, and very complete work-ups, including many serologic tests, had been made Owing to the fact that she could not speak English well and tended to call her bouts "gas pains," her appendix had been removed in 1943 In April 1946, because the gallbladder was poorly visualized, it was removed, the pathologist reported mild fibrosis Neither of these procedures was of the slightest benefit as far as the main symptom was concerned The situation had reached the point that the patient wanted her breast removed

For the last two years she had been having increasing difficulty in vision, tending to have diplopia at times in the last year She had had three normal children, who were all living and well

There were only a few points of pertinent interest in the examination 1 The patient had paresis of the right sixth cranial nerve 2 The reaction to light was sluggish in both eyes but especially in the right 3 The breasts revealed no abnormality 4 Other neurologic findings were not significant

As the patient had had complete gastrointestinal and cardiopulmonary examinations, with roentgenograms and electrocardiograms proving noninformative, it was decided to see if we were not dealing with one of Head's zones of referred pain Accordingly, a lumbar puncture was done for the first time on this patient on Feb 8, 1947, there was no increase in pressure One specimen of spinal fluid examined in the hospital laboratory gave a negative result in the Kahn test, the globulin content was 2 plus, and the Lange colloidal gold curve was 5543221000 A portion of the same specimen sent to the state laboratory gave a positive reaction to the Kahn test, there was no report on globulin, and the colloidal gold curve was 1123322110 As usual, all the serologic tests showed negative results

A tentative diagnosis of neurosyphilis was made, and, starting on February 15, an injection of iodobismitol® (a solution of bismuth sodium iodide and sodium iodide in propylene glycol containing saligenin and acetic acid) was given twice weekly on eight occasions Within three weeks the patient noted a definite diminution of the pain in the breast A total of four injections, each of 2 Gm, of tryparsamide U S P, was given weekly, starting March 19 This therapy was discontinued because, though there was almost complete disappearance of the pain, the vision became much poorer The patient had another course of injections of iodobismitol,® followed by four weekly injections of 45 mg of dichlorophenarsine hydrochloride U S P On June 18 spinal fluid obtained by lumbar puncture revealed 3 plus globulin and gave a negative result in the Kahn test and a colloidal gold curve of 0011211000

The patient refused to see an ophthalmologist In June, when an attempt was made to transfer her to a syphilologist nearer her home, treatment was discontinued

CONCLUSION

A case of pain in the breast due to neurosyphilis is presented, which is believed to be the first of its kind recorded in the literature

GRANULOMA CUTIS CALCINOSUM FOLLOWING INJECTION OF CALCIUM LEVULINATE

CHAIM BERLIN, M D
TEL-AVIV, ISRAEL

A peculiar local untoward incident following an intravenous injection of calcium levulinate came to my observation recently At the site of injection a nodular eruption, which took the appearance of granuloma annulare, developed

REPORT OF A CASE

M D, a boy aged 17, was admitted to the hospital in July 1945 because of peritoneal tuberculosis accompanied with ascites He was given roentgen therapy and intravenous injections of calcium levulinate, with much improvement in his condition Once during such an injection he experienced a painful sensation and slight local redness The physician, fearing a subcutaneous infiltration, stopped the injection immediately But no infiltration occurred, and the redness and tenderness subsided within several hours The next day, a papular eruption appeared at the site of injection When the patient was seen by me, six days after the incident, the left cubital area presented a plaque measuring 1 5 by 1 cm, consisting of pinhead-sized to match head-sized, slightly raised, firm, closely aggregated and partly coalesced nodules with smooth surfaces The color was pinkish to yellowish and became lighter on diascopic pressure The lesions were neither pruritic nor painful Most of the nodules were arranged in a horseshoe fashion, and the plaque closely resembled the picture of granuloma annulare (fig 1) No change was observed during the next two weeks The plaque was then totally excised, and the microscopic examination made by Dr Karplus confirmed the tentative diagnosis of deposits of calcium A report on the examination follows

"Corresponding to the nodules distinctly seen on gross observation, there were foreign body granulomas in the form of tubercles with many giant cells of middle size in the deeper layers of the cutis Most of the cells were fibroblasts, and there

From the Department of Dermatology, Hadassah Municipal Hospital

cells in the superficial portion of the corium Sharply circumscribed, rounded tubercles were present in the deeper portion of the corium These were composed of syncytial masses of lipid-laden epithelioid cells and a few Langhans' giant cells Lymphocytes were absent, and there were no signs of caseation There were no changes in the epidermis or superficial part of the corium to account for the clinical appearance of follicular papules, although serial sections of two biopsy specimens were studied The pathologic diagnosis was Boeck's sarcoid

Cutaneous lesions persisted unchanged during a two month observation period, which terminated when the patient had an acute schizophrenic episode, which necessitated her transfer to a psychiatric institution

COMMENT

In classifications of cutaneous tuberculosis such as that proposed by Michelson and Laymon,[7] prognosis has been determined by the clinical features of the eruption, and the results of histologic and immunologic studies have been considered of less importance The morphologic aspect of the lesion may, however, prove to be an unreliable index of prognosis On the basis of its clinical appearance, the eruption in the case under discussion was classifiable as a "form which tends to heal relatively rapidly" (lichen scrofulosorum), although laboratory studies, examinations of histologic structure and tuberculin testing suggested a chronic and progressive process Unquestionably, prognosis for the various types of tuberculids depends to a considerable extent on the resistance of the host to the underlying visceral tuberculosis Consideration of all the clinical, bacteriologic, immunologic and histologic findings in any given case is necessary for adequate evaluation of the patient's resistance The relative importance of each of these factors in determining prognosis has not yet been clearly defined, and emphasis on morphology or any other single factor is therefore unjustified In addition, numerous reports attest the fact that lichen scrofulosorum of typical gross and microscopic morphology may occur in conjunction with other tuberculous lesions, i e, lupus vulgaris, which have widely different prognostic significances

SUMMARY

A patient exhibiting lesions clinically typical of lichen scrofulosorum presented histologic and immunologic features of cutaneous sarcoid, as well as sarcoidal involvement of the uveal tract, salivary glands and lungs

Implications relative to the classification of cutaneous tuberculosis are discussed

6230 North Kenmore Avenue (40)

7 Michelson, H E, and Laymon, C W Classification of Tuberculosis of the Skin, Arch Dermat & Syph **52** 108 (Aug) 1945

Society Transactions

LOS ANGELES DERMATOLOGICAL SOCIETY

Maximilian E Obermayer, M D, *President*

Franklin I Ball, M D, *Secretary*

Feb 11, 1947

Mycosis Fungoides (with Vertebral Involvement, Treated with Nitrogen Mustard) Presented by DR BEN A NEWMAN

R G, a white woman aged 59, has had a recurrent generalized eczematoid dermatitis for the past eleven years This condition has been treated with several courses of roentgen radiation In 1945 a diagnosis of mycosis fungoides was made from a biopsy specimen During one and one-half years she received roentgen therapy, a course of diphtheria toxoid and injections of antireticular cytotoxic serum without benefit She was admitted to the hospital again on Nov 1, 1946 At that time, she presented a generalized dermatitis involving the entire cutaneous surface, consisting of eczematoid infiltration and plaques

The patient was given two courses of nitrogen mustard (three injections of 6 mg each) during a two week period One week after the first injection, involution of the lesions occurred and also pruritus At the end of three weeks her skin was entirely clear except for a bandlike vesicular patch extending across the right scapula and over the right breast When the vesicular patch became visible, after the generalized dermatitis disappeared, a diagnosis of herpes zoster was made Roentgenologic examination of the spine at this time showed a compression of the fourth dorsal vertebra

The blood cell count, urine and results of the blood chemistry determinations were normal

Mycosis Fungoides (Treated with Nitrogen Mustard) Presented by DR. BEN A NEWMAN

R C, a white woman aged 58, has had recurrent generalized pruritus for thirty years For the past three years, she has been under constant care at the Los Angeles County General Hospital and has been refractory to roentgen irradiation for the past year On Jan 2, 1947, she was admitted to the Cedars of Lebanon Hospital for nitrogen mustard therapy At that time, she presented a generalized eruption consisting of bright red, thick, scaly infiltrated patches

The infiltrate disappeared after three injections of nitrogen mustard, but further therapy was restricted because of a drop in the leukocyte count The pruritus has decreased considerably, and the infiltrated patches are now pinkish and softer

Mycosis Fungoides (Treated with Nitrogen Mustard) Presented by DR BEN A NEWMAN

F S, a white man aged 62, has had a chronic dermatitis of both hands for twelve years Since the beginning, he has had numerous attacks of a generalized eczematoid dermatitis. In each instance, roentgen irradiation was the only agent that produced involution of the eruption, in spite of considerable topical therapy

The present attack began three years ago with generalized eczematoid dermatitis During this period, the patient received repeated courses of low voltage roentgen

were only a few inflammatory elements Sections stained with hemalum and eosin revealed in the center broad, calcified, collagenous bundles (fig 2) The fundamental color of the tubercle was somewhat bluer than was that of the surrounding tissue A Kossa stain gave wide impregnation of silver in the fibers throughout the tubercle The nolular occurrence of the process indicated an embolic process, that is to say, during the injection calcium reached the skin through small arterioles"

COMMENT

This strange form of calcinosis is certainly extremely rare On the other hand, it is obvious from the history and the histologic observations that the eruption was a consequence of the injection of calcium levulinate However, nothing definite can be said about the mechanism of the eruption The passage of a calcium compound outside the vein usually produces severe, nonspecific, painful infiltration But in this case it must be assumed that even during the puncture particles of calcium succeeded in reaching the skin There they were dispersed, to cause the formation of reactive nodules

SUMMARY

A case of calcinosis of the skin following an intravenous injection of calcium levulinate is reported Around the site of the injection in the cubital fossa an immediate erythema, accompanied with pain, developed This rapidly subsided and was followed by a group of asymptomatic, small, firm, pinkish nodules, which, with their semicircular arrangement, resembled granuloma annulare Histologically, calcified collagenous bundles and foreign body giant cells were found

9 Montefiore

REACTIONS TO BISMUTH SODIUM TRIGLYCOLLAMATE (BISTRIMATE®)

LOTHAR WIRTH, M D
RENSSELAER, N Y

Bismuth sodium triglycollamate (bistrimate®), a new oral bismuth compound for oral administration, has been found effective in systemic bismuth therapy [1] Only minor side reactions, which were limited to the gastrointestinal tract, were observed—reactions which, after dosage had been temporarily reduced, did not interfere with continued administration of bismuth sodium triglycollamate [2] More recently, however, I saw 2 patients exhibit reactions to bismuth sodium triglycollamate which prevented continuation of treatment with this drug, although bismuth subsalicylate given parenterally was tolerated well I thought it might be worth while to report these cases

CASE 1.—A 70 year old man with tertiary syphilis of the central nervous system was started on treatment with bismuth sodium triglycollamate in the recommended dosage of 50 mg three times daily after meals On the third day of this regimen he exhibited an edematous lower lip, bluish discoloration of its mucosa

1 Lehman, R A, and Fassett, D W Experimental and Clinical Studies on Oral Bistrimate (Sodium Bismuth Triglycollamate) for Systemic Bismuth Therapy, Am J Syph, Gonor & Ven Dis **31** 640 (Nov) 1947

2 Gross, E R, and Wright, C S Oral Bismuth Therapy in Syphilis and Various Dermatoses, read before the Pennsylvania Medical Society, Philadelphia, Oct 8, 1946

irradiation with partial relief, but there were prompt recurrences on discontinuance of therapy During the past year, he lost about 15 pounds (7 Kg), chiefly from loss of sleep because of pruritus He was admitted to the hospital on Jan 25, 1947, for nitrogen mustard therapy

Physical examination revealed a generalized eruption consisting of patches and plaques of erythematous eczematoid lesions and erythematous dry infiltrated plaques

On February 3, treatment with nitrogen mustard was started He was given four intravenous injections of 6 mg each in five days On the sixth day, there was visible involution of the lesions and decrease in the itching The patient now presents some residual faint pinkish spots on the legs at the site of the former lesions Histologic examination of the tissue showed the typical polymorphous infiltrate with scattered histiocytes

DISCUSSION OF CASES OF MYCOSIS FUNGOIDES

DR L F X WILHELM I saw a great improvement in the woman who was at the County Hospital for a number of years, but the appearance of her lesions was not altered materially, and when I questioned her about the itching she said that it was still bad I think that we should see these patients again in thirty or sixty days

DR J R SCHOLTZ There appears to be no question that many of the patients treated with nitrogen mustard have been given symptomatic relief and that involution of the skin lesions is substantial Even though there is no assurance of the permanence of the results, the method certainly affords important palliative treatment in a difficult situation

DR A F HALL One patient denied having had any vesicles in the zoster area This zonal eruption appeared in the form of plaques which were themselves suggestive of mycosis fungoides It is of considerable interest to conjecture whether this is herpes zoster If it is, should one assume that it is due to the same virus that produces herpes zoster in otherwise well persons, or is this by any chance a zonal manifestation of mycosis fungoides, or, third, is it just that the eruption takes the form of mycosis fungoides in a person afflicted with that disease?

DR CLEMENT C COUNTER Is the fact that the patient had nausea and vomiting for two days after her injection considered sufficient reason for discontinuing administration of nitrogen mustard, or can it be used again in spite of this reaction?

DR BEN NEWMAN In reply to Dr Hall concerning the zoster-like distribution of the eruption in the first case, this patient had a generalized involvement of the skin with no clear areas except the palms, soles and face One week following a course of nitrogen mustard—methyl-*bis* (β chloroethyl) amine therapy, the entire skin was clear except for the wide patches of lesions that are now present Minute vesicles were scattered among these confluent, erythematous, eczematoid and slightly infiltrated plaques, following the course of the right fourth dorsal nerve The patient had been complaining of radicular pain in this area for two weeks, as well as generalized itching When I became aware of this new lesion, a roentgenogram was taken This showed a destruction of the fourth dorsal vertebra It has been my impression that this patient has a lymphomatous involvement of the vertebra, with radiculitis and herpes zoster, the zoster reaction in a skin already overwhelmed with mycosis fungoides was soon replaced by the lymphomatous response of the skin I believe that this lesion is mycosis fungoides, following a radicular distribution

and continuous salivation Food intake was very difficult Treatment with bismuth sodium triglycollamate was discontinued, and it took about ten days for the symptoms to subside It was then discovered that the patient had dissolved the tablets of the drug on his tongue, as he could not swallow pills Treatment was resumed, without ill effect, with parenteral administration of bismuth subsalicylate

CASE 2—A 55 year old man with syphilitic valvular heart disease was given bismuth sodium triglycollamate in the usual dosage He returned two weeks later with a generalized papulopustular eruption, which cleared within three weeks after treatment with the drug was discontinued Further treatment with bismuth sodium triglycollamate was then tried, at which time the eruption recurred After one month without therapy, treatment was resumed, without further difficulties, with bismuth subsalicylate administered intramuscularly

It seems appropriate to instruct patients not to dissolve bismuth sodium triglycollamate on their tongue, as this procedure undoubtedly predisposes to reactions within the oral cavity

I think the second case is unusual in that a cutaneous eruption occurred in a patient receiving bismuth sodium triglycollamate, while bismuth subsalicylate given parenterally was tolerated well

82 Broadway

PENICILLIN-RESISTANT EARLY SYPHILIS

Report of a Case

LOUIS WEXLER, M D *
AND
ROBERT N BUGG, M D *
NEW YORK

CAPTAIN HERBERT V ADAMS
AND
LIEUTENANT COLONEL ALLEN D SMITH
MEDICAL CORPS, ARMY OF THE UNITED STATES

Since the inauguration of penicillin therapy, resistant early infectious cases have rarely been encountered To our knowledge only 1 such case has been reported [1]

It is the purpose of this paper to present a case of penicillin-resistant early syphilis

REPORT OF A CASE

A 24 year old Negro was admitted to the Dermatology and Syphilology section on Sept 5, 1946 because of a penile lesion of six weeks' duration After appearance of the lesion no treatment had been sought for three weeks At that time the patient had received one intravenous injection of arsphenamine from a private physician, after which treatment the lesion became swollen and painful and did not heal No further treatment was obtained until his entrance to the hospital At admission, dark field examination revealed Treponema pallidum

From the Dermatology and Neurosyphilis Center, Oliver General Hospital, Augusta, Ga

* Formerly Captain, Medical Corps, Army of the United States

1 Tyson, W G Early Syphilis Resistant to Treatment with Penicillin Report of a Case, J Invest Dermat 6 279 (Oct) 1945

Nausea and vomiting usually cease after the first two injections The chief contraindication to further therapy is a significant drop in any of the elements of the blood

The patients presented this evening are part of a group of 6 patients with mycosis fungoides receiving treatment and under observation at the Cedars of Lebanon Hospital All the patients were roentgen-ray-resistant, and all have shown a favorable response to nitrogen mustard The degree of response has varied At present, my co-workers and I are studying various dosage and interval schedules of therapy I do not believe that nitrogen mustard will cure this disease, but it has already provided immeasurable relief to some patients With a chemical capable of destroying certain types of neoplastic cells, even temporarily, it is probable that we may be heralding an era of a new method of management (chemotherapeutic) of malignant disease

Darier-Roussy Sarcoid (Gumma?) Presented by DR STANLEY O CHAMBERS and DR STANLEY C ANDERSON

Granuloma Annulare of the Arms and Face. Presented by DR MOLLEURUS COUPERUS

Radiodermatitis with Ulceration (Successfully Treated with Radon Ointment) Presented by DR JUD R SCHOLTZ

Acrosclerosis (Favorable Response of Ulcers to Neostigmine Hydrobromide). Presented by DR MOLLEURUS COUPERUS

DISCUSSION

DR NELSON PAUL ANDERSON I am treating a patient with Reynaud's syndrome and sclerodactylia who has had ulcerations of the finger tips He weighs about 210 pounds (95 Kg) and is 6 feet 2 inches (188 cm) tall We have given him five injections of tetraethylammonium bromide It is apparently a potent drug, because shortly after the injection, which is given very slowly, he can feel increased warmth in the hands and feet and is able to move them with more freedom Just what the ultimate outcome will be, I cannot say, but I do feel that the treatment may at least lead to some useful information It may possibly give an indication as to which are the favorable cases for sympathectomy I doubt that this drug attacks the fundamental perivascular system itself In the October 1946 issue of *Surgery* there is an excellent article on this drug I warn you not to administer the drug when in a hurry, because it is necessary to spend an hour or two with the patient

A Case for Diagnosis (Carcinoma? Pseudoepitheliomatous Hyperplasia Associated with Infectious Mononucleosis and Primary Tuberculous Complex?) Presented by DR J WALTER WILSON

Psoriasis (Hypertrophic Lichen Planus?) Presented by DR NELSON PAUL ANDERSON

A Case for Diagnosis (Lupus Erythematosus?) Presented by DR H C L LINDSAY

and Kahn and Wassermann tests of the blood elicited positive reactions, a diagnosis of primary syphilis was made, and penicillin therapy was started, 100,000 units every three hours for eighty injections During the period that the patient was receiving therapy there was no improvement in the appearance of the chancre On the last day of treatment the prepuce became edematous and nonretractable, and concurrently a generalized, papular, erythematous, discrete, symmetric eruption appeared The papules ranged in size from that of a match head to that of a pea On the next day the eruption was more pronounced and more generalized Dark field examination of one of the papular lesions revealed it to contain living T pallidum, and the titer in the quantitative Kahn test at that time was 20 Kahn units

The patient was then started on a course of oxophenarsine hydrochloride (mapharsen®) and bismuth subsalicylate injections Two weeks later, after the patient had received four injections of oxophenarsine hydrochloride of 0 06 Gm each and two injections of bismuth subsalicylate, 0 2 Gm each, all cutaneous lesions had disappeared, and the titer in the Kahn test was 3 Kahn units At that time the patient was discharged with instructions to report to the local treatment center for completion of therapy, and further contact with the patient was lost

The penicillin used was a crystalline sodium penicillin supplied by the Army and of current stock, the lot number was not recorded at the ward However, concurrent usage in the cases of other patients with primary and secondary stages of syphilis revealed no further deviation from the expected result

SUMMARY AND CONCLUSIONS

A case of penicillin-resistant primary syphilis is presented After having received 8,000,000 units of penicillin, the patient acquired secondary syphilis After this development the response to heavy metal therapy in this case was very favorable

34 West Seventy-Fourth Street

ENDEMIC FAVUS IN TEXAS

BEN R EPPRIGHT, M D
AND
C H McCUISTION, M D
AUSTIN, TEXAS

A white woman aged about 36, consulted us on Nov 3, 1947, because of an eruption of the scalp, with loss of hair

She stated that the disease had begun about one year previously with localized scaliness and mild itching of the scalp The eruption gradually spread, the scaling became severer, and loss of hair ensued in the areas in which the eruption had been present the longest Although born in Poland, the patient had come to Texas twenty-five years ago and had not been out of the state since that time Both the patient and her parents stated that she had had no scalp disease of any kind prior to about a year ago and that no one else in the family had had any disease of the scalp She knows of no contact in the last few years with anyone from foreign countries

Examination revealed a woman of about the stated age, somewhat underweight The entire scalp was involved with scaling and numerous crusts and scutula The scutula were cup shaped, with the concave side facing upward Hairs, dull and

A Case for Diagnosis (Pigmentation of All Finger Tips from Unknown Extraneous Source, Factitious) Presented by Dr J Walter Wilson

A Case for Diagnosis (Dermatitis Vegetans?) Presented by Dr Samuel Ayres Jr

A Case for Diagnosis (Rhinophyma-like Eruption of Face? Lichenoid Eruption of Trunk?) Presented by Dr Samuel Ayres Jr

A Case for Diagnosis (Carcinoma of the Lip? Lupus Erythematosus?) Presented by Dr Thomas W Nisbet

A Case for Diagnosis (Erythema Induratum? Nodular Vasculitis?) Presented by Dr Nelson Paul Anderson

Maximilian Obermayer, M D, *President*

Franklin I Ball, M D, *Secretary*

March 11, 1947

Porokeratosis of Mibelli Presented by Dr Samuel Ayres Jr

N A a white boy aged 12, presents a lesion on the right side of the neck, approximately the size of a nickel with a narrow, elevated border which appears to be made up of individual elements showing dry, hyperkeratotic scaling along the top of the border The lesion developed about nine months ago There is one small pinhead-sized nodule within this circle, and there is a slightly lichenified appearance on the surface of the area enclosed by the ring

Histologic examination reveals that the most characteristic feature is in the epithelial layer, the central portion of which shows hyperkeratosis and parakeratosis with a follicle filled with keratin The prickle cell layer immediately surrounding the follicle is acanthotic, giving the appearance of a ridge with a furrow The basal cell layer is intact, with some perivascular infiltrate in the upper cutis

DISCUSSION

Dr Kenneth L Stout Clinically, I thought this was granuloma annulare, and when I looked at the section I found nothing to change my mind

Dr L H Winer I agree clinically with the diagnosis, but the histologic section did not show porokeratosis of Mibelli Of course, every section of porokeratosis of Mibelli would not necessarily show the characteristic histologic appearance Of interest in the slide are the porokeratotic scales These have been reported adjacent to the hyperkeratotic disks of porokeratosis of Mibelli and are located at the periphery of the disks of porokeratosis However, the infiltration of the cutis was deep and stellate in arrangement I could not see any collagenous necrosis I would suggest another biopsy

Dr Nelson Paul Anderson I think the slide is fairly typical of porokeratosis of Mibelli I think a good deal of variation is seen, depending on (1) the sites of biopsy and (2) where the actual slide is sectioned I happen to have Mibelli's original article on porokeratosis, and I am sure that from a number of photomicrographs in this article one would accept the section as typical

her closely but could get no history of the ingestion of arsenic I simply think that we have to decide whether this entire picture should be included in a single dermatologic entity, which I rather doubt at present

DR HAMILTON MONTGOMERY, Rochester, Minn I thought this was a case of congenital defect She has a flat nose You could not call it a congenital ectodermal defect with the changes in the tongue, but we have seen cases of endodermal and ectodermal changes merging together She did not have changes in the teeth but had changes in the palms that might indicate an ectodermal defect, as would the changes in the neck In addition she has apparently had a dermatitis which does not belong with that picture I would suggest that her family history be investigated

DR FRANCIS W LYNCH, St Paul, Minn I thought of the possibility of an ectodermal defect, but the mucosal changes were too great The family history is normal as far as could be learned on brief questioning

Darier's Disease (Keratosis Follicularis), Improvement Following Vitamin A Therapy Presented by DR S J ZAKON and (by invitation) DR A L GOLDBERG

A Case of Keratosis Follicularis with Cutaneous, Mucous Membrane and Nail Changes Presented by DR CLEVELAND J WHITE and (by invitation) DR ROBERT H HARRIS

A Case for Diagnosis (Drug Eruption? Neurotic Excoriations? Cutaneous Tuberculosis?) Presented by DR D V OMENS and (by invitation) DR H D OMENS and DR J GRAFFIN

A Case for Diagnosis (Sarcoidosis?) Presented by DR M H EBERT and (by invitation) DR ALLEN PEARL

Sarcoidosis Presented by DR STEPHEN ROTHMAN and (by invitation) DR EDWARD LADEN

Multiple Neurofibromatosis of Von Recklinghausen Presented by DR THEODORE CORNBLEET and (by invitation) DR D COHEN and DR J GRAFFIN

Multiple Neurofibromatosis Presented by DR EDWARD A OLIVER and staff of Hines Hospital

Rupial Syphilid Presented by DR D V OMENS and (by invitation) DR HAROLD D OMENS and DR N L BAKER

Secondary Syphilis and Granuloma Inguinale (?) Presented by DR JAMES R WEBSTER and DR S M BLUEFARB and (by invitation) DR N L BAKER

Chronic Urticaria Due to Intestinal Organisms, "Giardia Lamblia", "Cure" Following Treatment with Quinacrine Hydrochloride Presented by DR JAMES H MITCHELL and (by invitation) DR ROBERT H HARRIS

Folliculitis Decalvans (?) Presented by DR JAMES H MITCHELL and DR ROBERT H HARRIS (by invitation)

Folliculitis Decalvans Presented by DR F E SENEAR and staff

A Case for Diagnosis (Leprosy?) Presented by DR F E SENEAR

Linear Lichen Planus Presented by DR JAMES H MITCHELL and DR RALPH SCULL and (by invitation) DR BERNARD YAFFE

Epidermolysis Bullosa Presented by DR F E SENEAR and staff

Widespread Morphea with Acute Development Presented by DR STEPHEN ROTHMAN and (by invitation) DR LOUIS RUBIN

Two Cases for Diagnosis (Unrelated), (Lichen Sclerosis et Atrophicus?) Presented by DR THEODORE CORNBLEET

Eosinophilic Granuloma Presented by DR EDWARD A OLIVER and (by invitation) DR E LORANT

Pityriasis Rubra Pilaris Presented by DR S ROTHMAN and (by invitation) DR J H MCCREARY

Eczema Vaccinatum Presented by DR F E SENEAR and staff

A Case for Diagnosis (Secondary Vaccinia [Autoinoculation]) Presented by DR F E SENEAR and staff

DR SAMUEL AYRES JR My experience with this disease has been limited to 1 case, and in that instance total destruction was the only method that appeared to be successful—either excision or destruction, with electrodesiccation and curettage I think this is the method of choice

DR NELSON PAUL ANDERSON In Cleveland, at the last meeting of the Academy, Dr Cole showed a patient who had perhaps fifty lesions of porokeratosis of Mibelli around the face and neck Under moderate vitamin A dosage, 25,000 units three times a day, there had been at least a 75 per cent regression, according to the photographs and the condition of the patient Dr Allen in San Diego has a whole family with porokeratosis of Mibelli, with one patient who had ten to twelve lesions on the neck, and there has been dramatic improvement with vitamin A therapy

Chronic Urticaria of Seventeen Years' Duration Presented by DR NELSON PAUL ANDERSON

Tinea Capitis Favosa in a Girl Aged Eleven Years, a Native of the Island of Rhodes Presented by DR M E OBERMAYER and DR J WALTER WILSON

Favus of the Scalp Presented by DR HAROLD E ANDERSON and DR J WALTER WILSON

M K, a white woman aged 28, has had a fungus infection of the scalp continuously since infancy Nine siblings and two paternal aunts are said to have been similarly infected, in some of whom the infection is still present When the patient was 6, the entire family was treated at the Mayo Clinic with roentgen epilation, some were cured This patient states that such epilation was carried out three times in her case Many other attempts have been made at treatment, with uniform lack of success

Examination under Wood's light revealed a dull greenish fluorescence extending along numerous hair shafts for 2 to 3 cm from the scalp Potassium hydroxide preparations of such hairs showed hyphal threads within as well as around the hair shaft, together with chains of spores and occasional air bubbles Culture was obtained on Sabouraud's glucose agar, but only on the third attempt because of secondary involvement with bacterial and nonpathogenic fungi Sufficient growth has been obtained, however, to enable microscopic diagnosis of Trichophyton schoenleini to be made

No treatment has been instituted to date

DISCUSSION OF TWO PRECEDING CASES

DR H P JACOBSON I saw only 1 of the 2 cases The scalp lesions in that patient consisted of several roughly circular patches of inflammatory alopecia with some scarring but no scutula The culture is characteristic The presenter states that topical treatment has proved of no avail My therapeutic suggestion would be topical employment of 15 per cent thymol in oil of thyme The scalp should be shaved once a week, and the thymol application should be put on once daily with an applicator I have had success in the management of tinea capitis (microsporic and trichophytic) with this fungicidal agent

DR. L H WINER The first patient did not have scutula but did have the typical atrophic scars of favus In the second case scutula were present, and on being daubed with alcohol they became yellow, which is a characteristic of favus

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DR H C L LINDSAY In 1913 Dr Sabouraud showed some patients who had had favus since their earliest days He stated that he had treated the parents of these patients for favus and, furthermore, that in a study of the records of St Louis Hospital, Paris, it was possible to prove that favus had been present in the ancestors of these patients for generations At this time Dr Sabouraud was epilating the scalp of patients with favus with roentgen rays as a preliminary treatment Success in treatment of favus among illiterate persons is most difficult Fortunately, hairs in which favus is growing are not so brittle as when they are invaded by small-spored ringworm Thus favus hairs can be plucked manually Favus was not infrequently seen at St Louis Hospital, and a considerable number of the patients had permanent scars and alopecia in patches

DR CLEMENT E COUNTER Is the temporary epilation of the scalp expected to cure favus? One of these patients presented tonight has had epilation three times She still has the disease

DR BEN NEWMAN In reference to temporary roentgen ray depilation, our attention should be directed to two important considerations one, that in the past number of weeks approximately a dozen cases of Microsporum audouini infection of the scalp have been uncovered in and around Los Angeles and that we may expect an epidemic form of the disease, if the same pattern is followed here as has occurred in all the larger cities throughout the county, two, that heretofore it has not been necessary, nor has it been the custom, to employ roentgen ray depilation in the treatment of tinea capitis in this area Hence, if we desire to control the spread of this epidemic, we must recognize the need for such depilation and establish this procedure as a proper and customary type of therapy in this community to avoid medicolegal complications Certainly, the merits and need for depilation in Microsporon audouini infections of the scalp require no discussion among dermatologists

DR H C L LINDSAY A few years ago efforts to demonstrate favus fungus in hairs by stain were not always successful Hot carbolfuchsin was used to stain, and dilute nitric acid was used to decolorize Supposedly the decolorizing of the fungi should be slower than that of the other stained material Unfortunately, the hair would decolorize at approximately the same speed Accidentally, I placed some partially decolorized stained hairs containing favus in a watch-glass container which was partially filled with aniline oil I forgot about these hairs for a week When I examined them with the microscope, the fungus in certain parts could be seen retaining the dye, while the rest of the field was clear

DR NELSON PAUL ANDERSON No one has ever seen favus develop in an adult If complete epilation had been carried out on this woman and the disease cured, she would not have been reinfected when an adult Sabouraud said he had never seen a case of favus transferred to an adult I am convinced that certain types of favus are curable by manual epilation I have had 3 cases of favus, 1 involving the thumbnail, 1 involving the scalp of a little girl and 1 involving the scalp of the aunt of the little girl The mother faithfully epilated all the hairs from the scalp of the daughter and faithfully scraped her own thumb nail Both patients are now well The scalp of the maternal aunt still presents widespread involvement

DR J WALTER WILSON I am glad that Dr Obermayer and Dr Anderson afforded me the opportunity of carrying out the mycologic studies in these 2 cases, which I believe are representative of favus under treatment and scrupulous cleanliness Growth of T schoenleini was obtained only with difficulty from the adult because of the presence of other nonpathogenic fungi, which repeatedly suppressed

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its growth The dull greenish fluorescence extending for 2 or 3 cm distally along the hair shaft is typical The adult is able to trace the disease through her father to his parents, who came from Luxembourg, the child's parents came from the Island of Rhodes

DR HAROLD E ANDERSON My patient, the adult in the second case, had much heavy, dry scaling extending along and matting together the hair shafts when I first saw her It reminded me of what is called tinea amiantacea A microscopic examination of potassium hydroxide preparation of hairs and scales selected for study revealed numerous mycelia and spores Secondary invaders overgrew the culture mediums, but Dr Wilson was finally able to isolate T schoenleini The familial tendency, the clinical appearance and the cultural study all are typical of tinea favosa She has already had roentgen ray epilation at least three times, once at the Mayo Clinic and once at the University of Iowa She was treated at the Mayo Clinic in 1924 A direct microscopic examination of hairs at that time revealed fungi, but the result of the cultural study was not reported The postepilation therapy was carried out at home in Iowa, and apparently the parents were not diligent enough with this therapy

Basal Cell Epithelioma (Morphea Type) Presented by DR SAMUEL AYRES JR and DR JOSEPH I MIROVICH

DISCUSSION

DR A F HALL In several cases in which I have tried treatment by radiation the condition has proved recalcitrant, I think the lesion has to be destroyed in some other way, such as by cautery

DR ANKER K JENSEN At the risk of repetition, I would again say that in the management of cutaneous malignant growth we must carry out the radical measures first Conservative management is at no time justified in the handling of cutaneous neoplastic disease This applies both to radiation therapy and to surgical procedures I confess partiality to cautery surgery, but of course I am also employing radiation My radiation dosages are much heavier than those employed in the present case I am inclined to agree with Dr Hall that the epithelioma in our present patient has the aspects of a morphea-like lesion, and this could possibly be a factor in its apparent radioresistance There is, of course, little if any danger of distant metastasis from this lesion, it being a basal cell growth The clinical picture at present, however, indicates a steady but progressive extension and activity, and unless eradicated completely it will probably result in a rodent ulcer I recommend radical surgical treatment by means of cautery

DR L H WINER Basal cell carcinomas of the scalp are occasionally of sebaceous gland origin and as such are radioresistant I agree with the preceding discussers that excision followed by skin graft is the treatment method of choice

Blastomycosis of the Foot (North American) Presented by DR W H GOECKERMAN, DR L F X WILHELM and DR MORLEURUS COUPERUS

Acanthosis Nigricans Presented by DR NELSON PAUL ANDERSON

J H D, a white youth aged 18, had a pinkish eruption under the arms, on the sides of the trunk and on the abdomen about three years ago Physical examination at the present time reveals a rough, elevated, dirty brownish reticu-

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Histologic examination of the tissue showed a verrucous acanthotic process, with one area where there were four nests of cells just beneath the epidermis, like a nest of melanoma cells Many of the epidermal cells were vacuolated

Treatment has consisted of administration of massive doses of vitamin A, with great improvement The patient has recently been using sodium thiosulfate soaks at the suggestion of Dr E S Lain, of Oklahoma City

DISCUSSION

DR L H WINER My clinical impression was the close resemblance of this case to parapsoriasis, especially in regard to the lesions on the abdomen and flanks However, the verrucous lesions in the right axilla were characteristic clinically of acanthosis nigricans, as was the histologic section Histologically, one cannot differentiate the benign form from the malignant form of acanthosis nigricans

Urticaria Pigmentosa Presented by DR STANLEY O CHAMBERS and DR STANLEY C ANDERSON

Verruca Plana of the Face Treated by Posthypnotic Suggestion Presented by DR MAXIMILIAN E OBERMAYER

D P, an unmarried woman aged 21, noticed the appearance of a group of flat warts on the right side of her chin two years ago The dermatologist who was treating her at that time with fractional doses of roentgen rays for acne vulgaris intimated that the warts would probably disappear with continuation of treatment However, the verrucae spread rapidly, and when the course of roentgen therapy had been completed they involved most of the face Various dermatologists removed the ordinary warts which appeared on the fingers of the right hand by means of electrodesiccation Injections of bismuth subsalicylate in oil, given over a period of eight months, as well as subsequent applications of peeling ointments and solid carbon dioxide and the use of lotions in combination with ultraviolet irradiation, had no effect on the verrucae planae of the face

When I saw the patient for the first time, on Dec 5, 1946, her face was studded with verrucae of the flat juvenile type and lesions were also present on the forehead, the anterior portion of the scalp and the sides of the neck Most of the right side of the face and neck was covered with confluent plaques, while the lesions on the left side were more scattered

When it became clear that the oral administration of bismuth (sobisminol mass) and the local use of a 20 per cent solution of podophyllin in acetone had failed to benefit the patient, her mother was told that I had no other therapeutic suggestions, and the irrational behavior of warts was discussed and illustrated by an account of Dr Bloch's experiments in Zurich A few days after this discussion, the mother suggested that arrangements be made for treatment by posthypnotic suggestion I agreed In order to complete my record of the case, biopsy of a lesion was performed The section showed the features typical of verruca plana juvenilis

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The patient was then referred to Dr Ralph R Greenson, certified by the American Board of Psychiatry She saw Dr Greenson only three times, at weekly intervals Two weeks after the last consultation, in accordance with a suggestion made during light hypnotic sleep, all verrucae had disappeared

The skin today reveals no trace of the lesions

DISCUSSION

DR A F HALL I think we will all admit that the warts either went away spontaneously or were cured by suggestion, to believe the former demands too much of coincidence I think we will admit that Rasputin, the "black monk of Russia," controlled the czarevitch's hemophilia by suggestion I think most of us, if not all, can cite examples of warts that have been cured by prayer or wishing or out and out suggestion, either in our childhood or in our practice, since Bloch put this type of treatment on a respectable basis, I expect that "suggestion" is the proper word It is intriguing to conjecture regarding the mechanism involved I remember seeing an article on the subject by Karl Zwick in the ARCHIVES (Zwick, K Hygiogenesis of Warts Disappearing Without Topical Medication, *Arch Dermat & Syph* **25** 508 [March] 1932) The author's conjecture is that the treatment of warts by magic and suggestion often includes traumatism of the wart, e g, by rubbing it with a potato or a penny or an apple He also mentions the cure of warts by suggestion without touching the wart He feels that the factor which the two types of approach have in common is perhaps that the wart is unfavorably affected by tissue juices, he advances this theory, because in the inoculation of warts, if any of the innoculum gets into the subcutaneous tissue, a new wart will not appear He further points out that, by psychic methods, extravasation of serum and diapedesis of blood cells can take place under hypnosis He thinks it is through some such mechanism as this that warts may be influenced Were I to "take it from there," I should hypothecate that if there is a tissue fluid or some substance in the corium inimical to warts, it may be the same substance that makes the difference between the bleeding of ordinary tissue and the bleeding of a wart The prolonged bleeding time, seen when a wart is cut, may be due to the absence of thromboplastin in warty tissue, it may be this substance, present in the corium and absent in warts, that is inimical to the "life" of a wart One might try injection of thromboplastin into the base of a wart as treatment, in circumstances which would eliminate the factor of suggestion

DR J R SCHOLTZ In my opinion, most of the treatments that we use for warts act by suggestion, and as far as I am concerned, treatments which are harmless and do not leave scars are the most desirable I can see no therapeutic sense in using any method which causes a scar in place of a benign, harmless lesion There is no doubt that psychotherapeutic methods are effective in the treatment of warts Recently in the clinic of the Los Angeles County Hospital, a boy aged 8 years was seen with four to six large verrucae vulgares on his hands They were bright blue, and it was found that he had been treating them daily with an indelible pencil We encouraged him to continue and stated that the warts would probably disappear in about three weeks On his return a month later, all the warts were gone

DR MAXIMILIAN OBERMAYER There are two reasons for this presentation First, I believe that dermatologists should become better acquainted with the extraordinary fact that an infectious disorder may be amenable to suggestive therapy Obviously, first hand knowledge of the data in an authenticated case

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will be much more enlightening than information obtained by hearsay or from an unassimilated skimming of psychiatric literature, as the late Dr Bloch fully realized when he conducted his now famous clinical experiment with Swiss school children Second, I believe that speculation about the nature of the working mechanism underlying the indisputable results of suggestive therapy will prove of value In my opinion, it is most rational to assume that the neurovascular mechanism is involved The psychodynamic factors which lead to contraction of the capillary vessels and consequent pallor in certain emotional states are perfectly familiar Logically one may assume, then, that suggestion can produce a similar spasm of the capillaries, with consequent shutting off of the blood supply to the lesions Dr Greenson approached the problem with such an assumption in mind

Since a preliminary interview revealed no psychoneurotic features, the psychiatrist expressed the belief that while the treatment could produce no ill effects, its chance of success was small At the end of the first interview, the patient was told to imagine for a few minutes before bedtime each night that her face was covered by cold compresses and was beginning to itch and tingle At her second visit, she gave the encouraging report that she had had the sensation of itching An attempt at hypnosis was followed only by a state of deep relaxation without sleep, during which it was suggested that her face would feel cold, her skin would itch and the warts would begin to fall off The patient began the third and last consultation by stating that the warts had commenced to become scaly Once more hypnosis was attempted, and a state of light sleep was produced It was then suggested that her face would feel cold and turn pale and that the lesions would itch and fall off within two weeks The patient was awakened and told that no further interviews were contemplated because her warts would shortly disappear Two weeks later her skin was clear of all lesions

I should be the last to propose that posthypnotic suggestion be employed routinely in the treatment of verrucae On the other hand, since the shortcomings and unreliability of all the so-called approved methods of treating warts are well known, I believe that suggestive therapy should be given a trial when conventional methods have proved useless and extensive involvement has raised a problem from the cosmetic standpoint, as in this case That such therapy will succeed with only a limited number of patients is obvious and that it should be carried out only by a fully trained psychiatrist well versed in the technic and aware of the dangers of hypnotic suggestion is equally clear Certainly most dermatologists would willingly accept a dozen failures with psychotherapy rather than invite a single instance of the dermatitis actinica produced by roentgen therapy The sooner suggestive therapy is given a fair and unbiased trial by the dermatologic profession the sooner its limitations and suitability will be established

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CLEVELAND DERMATOLOGICAL SOCIETY

Harley A Haynes, M D, *President*

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March 27, 1947

Lymphogranuloma Venereum of the Shaft of the Penis, Nodules and Sinuses Presented by DR H H JOHNSON and DR A M TANNO (by invitation)

A Case for Diagnosis (Tuberculous Cervical Lymphadenitis? Lupus Miliaris Disseminatus? Tuberculid?) Presented by DR H H JOHNSON and DR A M TANNO (by invitation)

Pityriasis Rubra Pilaris? Presented by DR J KAM, DR R C LIGHT and DR A E WALKER (Service of DR H N COLE and DR J R DRIVER)

A Case for Diagnosis (Chronic Dissecting Cellulitis of the Groin and Left Foot Resembling Deep Mycosis?) Presented by DR J KAM, DR R C LIGHT and DR A E WALKER (Service of DR H N COLE and DR J R DRIVER)

Diffuse Progressive Scleroderma Presented by DR J KAM, DR R C LIGHT and DR A E WALKER (Service of DR H N COLE and DR J R DRIVER)

Perifolliculitis Abscedens et Suffoidiens Capitis (Hoffman) Presented by DR J KAM, DR R C LIGHT and DR A E WALKER (Service of DR H N COLE and DR J R DRIVER)

DISCUSSION

DR R C LIGHT There was pronounced improvement after the patient received two treatments of filtered roentgen rays

DR J R DRIVER I should like to ask whether any of the members have treated a condition of this kind with penicillin by injection and what the result has been

DR G H CURTIS I saw 2 patients in the Army treated with 8,000,000 units of penicillin without any benefit

DR H N COLE There were several of these patients at City Hospital, with chronic conditions They were given penicillin by injection and also treated locally with penicillin and penicillin irrigations, without any effect The disease in this case is relatively recent, which I believe is the explanation for the response

Severe Generalized Excoriations Associated with Jaundice (Possible Xanthomatous Biliary Cirrhosis) Presented by DR J KAM, DR R C LIGHT and DR A F WALKER (Service of DR H N COLE and DR J R DRIVER)

1 **Boeck's Sarcoid** 2 **Early Latent Syphilis, Partially Treated** Presented by DR J KAM, DR R C LIGHT and DR A E WALKER (Service of DR H N COLE and DR J R DRIVER)

A Case for Diagnosis (Dermatitis Repens?) Presented by DR H H JOHNSON and DR A M TANNO (by invitation)

Alopecia Liminaris Frontalis (Sabouraud) Presented by DR J KAM, DR R C LIGHT and DR A E WALKER (Service of DR H N COLE and DR J R DRIVER)

F W, a Negro woman aged 28, first noticed mild acne of the face and the gradual onset of alopecia of the frontal region of the head in October 1945 Within several months this reached its peak and has persisted to the present There is no history indicative of an endocrine disturbance She has used petrolatum on her hair for many years There is no family history of similar disease

Results of a general physical examination were normal, and she appears in good condition In the frontal portion of the scalp there is a symmetric, well defined band which is almost completely devoid of hair This extends from ear to ear and 3 to 5 cm back of the hair line There is conspicuous plugging of the follicles throughout, and the skin is slightly depressed, suggesting atrophy No erythema is seen There is mild papular acne of the face

Observations in hemograms and urinalyses were normal The result of the serologic test for syphilis was negative The basal metabolic rate was +16 per cent

On histologic examination, the epithelium showed no significant change There was a scattered infiltrate of lymphocytes, histiocytes and pigmented mononuclear cells in the upper part of the corium and to a lesser extent in a few deeper areas around the hair follicles Keratotic plugs often blocked the mouth of the follicles, which frequently contained no hair A trial course of 100,000 units of vitamin A daily for two months had no objective effect

DISCUSSION

DR H G MISKJIAN I have been interested in this subject for some years, after I read a long description of the syndrome given in the *Annales de dermatologie et de syphiligraphie* in 1931 by Sabouraud, in which he said that he had seen 12 cases of this disease in thirty years In the last ten or more years my co-workers and I have, here at the Lakeside Clinic, seen at least 10 or 12 cases, which were all in Negro women, and as far as I remember, all of them were in adults Sabouraud saw his cases in girls of acne age, about 15 to 18, and he mentioned a woman about 50 years old who had it, I have brought the book in which the picture of that woman appears This shows that there are differences between what Sabouraud reported and what we have seen here One of the differences is that in the syndrome we have seen the disease seems to be much more frequent than Sabouraud reported The second point of difference is that our cases are in adults and Sabouraud's were almost entirely in adolescents A third difference is in frequency, we have seen them much more frequently at our clinic The description seems to correspond closely with that of Sabouraud A patch of alopecia would develop on each preauricular temporal region, which would secondarily spread onto the forehead, toward the midline, with a band of alopecia about 1 inch (2 5 cm) or a little less Right on the fringe of the forehead and the band of alopecia there is usually a thin line of hair The patient presented today had that also The alopecia is supposed to be permanent, once it has been estab-

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DR W R HUBLER I do not believe that she has pemphigus There are numerous, annular, bullous lesions on the face and shoulders The symmetric distribution of the eruption and the localization on the neck, axillas, elbows, knees and shoulders, as well as the grouping of the lesions, all point to a herpetiform type of eruption The patient is Rh negative, the husband Rh positive, and she is beginning to have anti-Rh antibodies About six months ago she was hospitalized by a gynecologist for what was apparently an early spontaneous abortion This would account for the early rise in anti-Rh titer I do not know what the Rh titer has to do with herpes gestationis, but I feel that some factor might be implicated since it usually clears with termination of pregnancy Therapeutic abortion should be performed in this case, because in a number of cases in which the patients were allowed to go to term, the percentage of monstrosities among living children was much higher than normal and stillbirths were common (Mueller, C *Am J Obst & Gynec* **48** 170-180 [Aug] 1944) Also, in some cases the herpetiform eruption persists after the completion of pregnancy when the patient is allowed to go to full term

NOTE—The follow-up examination of August 1947 showed that the eruption had subsided strikingly after a therapeutic abortion However, punctate, small vesicles persist in the groin and axillas, on the chin and in other scattered areas These are subsiding with inorganic arsenical therapy Hyperpigmentation has developed further showing the relationship to dermatitis herpetiformis The anti-Rh titer, three months after the therapeutic abortion, is only 1 1

Extensive Circumscribed Myxedema Presented by DR M J GIBANS, Akron, Ohio

H O , aged 56, was subjected to a subtotal thyroidectomy in February 1945 because of a toxic goiter Preoperatively the basal metabolic rate varied from +72 to +79 per cent, and the blood pressure was 154 systolic and 84 diastolic Postoperative examinations showed metabolic rates of +27 and +40 per cent, and finally —15 per cent, and the blood pressure was 130 systolic and 70 diastolic His weight, which had been 130 pounds (59 Kg) before operation, increased to 179 pounds (81 Kg) thereafter About four months after operation, the patient noticed a little discoloration and redness about the ankles This progressed slowly until some months later, after he had returned to work, when it extended rapidly This has never caused him any discomfort

He now has nonpitting, tawny, elevated, nodular plaques, with moderately enlarged follicular openings, on the anterior aspects of both legs These plaques are much more extensive on the right leg, involving almost the entire lower half and extending over the medial surface and posteriorly, where there is one unusually large and firm mass, about 2 inches (5 cm) in diameter

The microscopic description by Dr Lloyd Catron was as follows There are slightly increased deposits of melanin in the epidermis, with edema of the corium The hair follicles are dilated and plugged with keratohyaline material The small blood vessels are thick walled There is a patchy infiltrate, composed chiefly of lymphocytes, around accessory skin structures The histologic appearances are compatible with circumscribed myxedema The patient has recently been given thyroid extract, 2 grains (130 mg) daily

Bullous Eruption (Pemphigus) Presented by DR E GILLESPIE, Canton, Ohio

Dermatitis Herpetiformis (?) in a Seven Year Old Girl Presented by DR H A HAYNES JR

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Acrodermatitis Chronica Atrophicans Presented by DR A E WALKER and DR W MARMELZAT (service of DR H N COLE and DR J R DRIVER)

Scleredema Adultorum (Buschke) Presented by DR A E WALKER and DR W MARMELZAT (service of DR H N COLE and DR J R DRIVER)

L S, a 51 year old Italian woman, had, approximately twenty months ago, a sudden onset of nonpruritic thickening and tightening of the skin of the neck, which spread to the lateral and anterior portions of the neck, the lateral aspects of the face, back, shoulders, upper arms and upper part of the chest The skin is softer now than it was after onset of the condition The patient has had previous episodes of infection of the upper part of the respiratory tract and influenza but no clearcut episode immediately preceding the onset of her present illness (There is a language barrier and a lucid history is difficult to obtain)

The patient has diabetes mellitus, which is being treated by diet and insulin She also has been treated medically for a hypertrophic arthritis Two years ago she had menorrhagia, the cause of which was never explained

There is painless, nonpruritic thickening of the skin of the back of the neck, extending over the dorsum to the iliac area, laterally around the neck to the anterior aspect, over the shoulders and upper arms to the deltoid area, and over the upper part of the chest and superior portion of both breasts The epidermis is not changed There is no pitting edema There are bilateral xanthelasma lesions

Urinalysis showed sugar (4 plus) and acetone (3 plus) The urea nitrogen was 18 mg per hundred cubic centimeters The fasting blood sugar was 303 mg per hundred cubic centimeters Total proteins were 6 3 Gm per hundred cubic centimeters—albumin 3 8 Gm and globulin 2 5 mg, combining power 52 5 milliequivalents per liter, blood cholesterol 354 mg, serum calcium 9 8 mg and serum phosphorus 4 3 mg per hundred cubic centimeters Results of hemocytologic studies were normal The blood and spinal fluid were normal The basal metabolic rate was +17 per cent Roentgenograms of the chest, sinuses, jaw and skull were normal

Biopsy of the skin revealed the epidermis to be normal The corium was thickened, made up of deeply acidophilic, greatly hypertrophied collagenous fibers The small vessels and capillaries were not remarkable but were surrounded by a moderate infiltration of lymphocytes and occasional polymophonuclear leukocytes No treatment has been given

DISCUSSION

DR H A BRUNSTING What is the duration of the disease?

DR R C LIGHT In the *New England Journal of Medicine* several months ago there was a report of a case of twenty years' duration

DR A E WALKER Another review I saw listed 1 case lasting thirty years and 1 four years The average is eight to eighteen months

Sarcoidosis (Granuloma Annulare [?] of the Elbows and Knees) Presented by DR A E WALKER and DR W MARMELZAT (service of DR H N COLE and DR J R DRIVER)

Sarcoidosis (Keloidal Lesions on the Nape of the Neck) Presented by DR A E WALKER and DR W MARMELZAT (service of DR H N COLE and DR J R DRIVER)

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Penicillin was administered, with pronounced diminution of the secondary infection The patient was transferred to Sunny Acres, Cuyahoga County Tuberculosis Hospital, for treatment of her tuberculosis

A Case for Diagnosis (Granuloma Telangiectaticum?) Presented by DR M H GUSTAFSON, DR E H JONES JR and DR UTTERBACH (service of DR H R TRATTNER)

G S, a 50 year old man, was first seen on the urologic service in September 1947, with a complaint of numerous growths on the penis and the scrotum, of two years' duration The lesions started as a papule on the dorsum of the penis and gradually increased in number and size, finally involving the entire penis, the scrotum, the perineum and the perianal area The lesions have been asymptomatic

The patient gave a history of having had gonorrhea in 1929 A urethral stricture developed in 1932 In 1933 the first of a series of urinary fistulas appeared, and since that time numerous fistulas have developed around the base of the penis, the scrotum, the lower part of the abdomen and the perineum

The shaft of the penis, the scrotum, the perineum and the perianal area are covered with a fungating, polypoid mass The surface of the mass presents numerous flesh-colored nodules, pedunculated tumors ranging from a few millimeters to 3 cm in diameter Several fistulous openings may be identified in the crevices between the polyps Urethral strictures are present, preventing the passage of sounds

Results of urinalysis and the hemogram were normal The blood urea nitrogen was within normal limits The Kline and Wassermann reactions of the blood were negative Reactions to the Frei test and to skin tests for chancroid were negative An intravenous pyelogram revealed a normal right kidney and ureter, the left kidney was poorly visualized There was a slight hydroureter in the lower portion of the left ureter Suprapubic cystostomy revealed a normal bladder

Histologic examination showed stratified squamous epithelium, the seat of chronic inflammation, with fibrosis of the corium and areas of acute inflammation with focal ulceration

Treatment has consisted of the administration of penicillin and suprapubic cystostomy in preparation for plastic repair

DISCUSSION OF PRECEDING CASES

DR G A DEORDO I think that both of the preceding cases are manifestations of lymphostasis, associated with lymphatic blockage, in the woman due to tuberculosis and in the man resulting from obliteration of the lymphatics by some chronic inflammatory process associated with his gonorrheal infection Clinically at least, the growths looked like lymphangiomas, a form of elephantiasis Microscopically, the picture in the man looked considerably different There are many dilated capillaries or possibly lymphatics with thicker walls I should offer the diagnosis of elephantiasis or lymphangioma in both cases

DR F M MACDONALD I have never seen elephantiasis due to granuloma inguinale This is not the usual picture, but for the sake of work-up it is a very unusual situation I did not see any reference made to examination for possible Donovan bodies Perhaps that was done and I did not see mention of it on the report

DR J E RAUSCHKOLB The case of A S is a lymphostatic type of disorder, that contention is proved There are elevated little cystic lesions, and the lymphostasis probably arises from a chronic inflammatory pelvic condition, which we assume to be of a tuberculous origin

lished, and one is supposed to see in the bald area small cicatricial lesions, which I was not able to see in this case I think it would be a very worth while contribution to bring together all of these cases to study them and point out that this syndrome is perhaps more frequent in the Negroes than in white person Nothing is known about it, because Sabouraud seemed to think that the syndrome must be placed between what he calls staretoid baldness, in other words alopecia, and an acneform process, because in the early stages he was able to see acne lesions in areas which later became bald There is a good description of this syndrome in Dr Sutton's book, "Diseases of the Skin," which is accurate

DR J A GAMMEL A few months ago I had a Negro woman patient with what I called alopecia areata, limited to the same areas, which cleared up very well in three months

DR H G MISKJIAN When this patient first came to us we considered the diagnosis of alopecia areata, because the case was not so very characteristic, and we ruled it out at that time At the present time the appearance is not that of alopecia areata There are thin areas that one would ordinarily not see in alopecia areata

DR J A GAMMEL I do not want to make a diagnosis in this case, but merely comment that I saw one with the disease limited to these areas There was complete baldness for two weeks, and in three months the whole process was over

DR H H JOHNSON There is one thing that Negro women do that is peculiar to their race, and that is using various methods of attempting to straighten hair I believe that that should be investigated thoroughly to find out what methods they use to accomplish it

A Case for Diagnosis (Lichen Planus Atrophicus? Chronic Atrophic Lichenoid Dermatitis [Csillag]? Retiform Parapsoriasis?) Presented by DR G W BINKLEY and DR H H JOHNSON

Papulonecrotic Tuberculid Presented by DR J KAM, DR R C LIGHT and DR A E WALKER (Service of DR H N COLE and DR J R DRIVER)

Harley A Haynes, M D, *President*

George W Binkley, M D, *Secretary*

May 22, 1947

Herpes Gestationis Presented by DR W R HUBLER, Youngstown, Ohio

DISCUSSION

DR J E RAUSCHKOLB This patient has neither oral nor ocular lesions She is two or three months pregnant In spite of this eruption having followed the beginning of pregnancy, I believe that the case is one of pemphigus vegetans because of the extreme prostration and toxicity and the grouping of the bullae on the neck band and axillary and genital areas, which are beginning to pile up and vegetate

DR C G LA ROCCO I agree with Dr Rauschkolb

DR J R DRIVER I agree with the diagnosis as presented There was no Nickolsky sign The woman is pregnant and has had this eruption since her pregnancy started A therapeutic abortion is indicated

Histologic examination showed pronounced hyperkeratosis, unusual prominence of the stratum granulosum, acanthosis and superficial chronic perivascular inflammatory infiltration of the corium

Since follow-up antisyphilitic therapy was instituted with bismuth subsalicylate, the patient says that the lesions have regressed for the first time

DISCUSSION

DR M UTTERBACH This patient gave a history of similar lesions in other members of her family, which I think is significant It is difficult to evaluate the lesions themselves We considered diagnosis of acrokeratosis, hydrokeratosis and perhaps linear nevus Biopsy showed definite proliferation of the corium Therefore we thought of the possibility of an acrokeratosis

DR H A HAYNES JR I have never seen a case like this, but the disorder could be verruca plana, inasmuch as it is undergoing involution with therapy

DR H J PARKHURST I thought that clinically on close inspection these do not appear to be ordinary warts They resemble the lesions in a case which I previously saw of epidermodysplasia verruciformis

DR G W BINKLEY It would be interesting to get a progress note on this case

Scleroderma, Acrosclerosis Presented by DR M H GUSTAFSON, DR E H JONES JR and DR UTTERBACH (service of DR J E RAUSCHKOLB and DR G A DEOREO)

George W Binkley, M D, *President*

George H Curtis, M D, *Secretary*

Gerard A DeOreo, M D, *Reporter*

Nov 20, 1947

Glossitis Rhomboidea Mediana Presented by Dr BENJAMIN P PERSKY

A Case for Diagnosis (Palmar and Plantar Keratoses [Arsenic?] [Keratoderma Disseminatum Palmaris et Plantaris]? Superficial Epitheliomas, Trunk Ulceration, Left Small Toe and Left Palm [Squamous Cell Epithelioma?]) Presented by DR B LEVINE, DR B PERSKY and DR I L SCHONBERG

A Case for Diagnosis (Ulcer, Penis, Cause Undetermined? Erythroplasia of Queyrat? Intraepidermal Epithelioma?) Presented by DR H H JOHNSON and DR I L SCHONBERG

J T, a Negro aged 32, was circumcised in February 1945, since which time there has been a superficial ulcer on the glans penis He has been hospitalized on numerous occasions since 1945 because of this penile lesion The treatment has included the administration of penicillin and numerous local medications, without any signs of improvement during this two year period

On admission to the service in May 1944 the patient was found to have a positive serologic reaction and was treated with a series of injections in the arm and the hip In 1945 he received 146 injections of penicillin because of the positive

Circumscribed Scleroderma Presented by DR F M MCDONALD, Akron, Ahio

Lichen Striatus Involving the Leg of a Four Year Old Girl Presented by DR F M MCDONALD, Akron, Ohio

Porokeratosis of Mibelli Presented by DR C L BASKIN, Akron, Ohio

T N, a 70 year old man, a native of Italy, came to the United States forty-five years ago His inability to understand the English language prevents a complete history in this case His general health has always been good, he has never lost time from work

The present eruption began when he was a small child, gradually spreading from a spot on the left calf to include the entire leg and a large area of the sole The lesions show the characteristic threadlike border and polycyclic configuration There has been a slow steady advance of the margins during these many years All laboratory examinations showed normal values

DISCUSSION

DR G W BINKLEY This is a giant form of porokeratosis of Mibelli In addition to the appearance of the lesion, the long duration and the patient's Italian nationality are points in favor of a diagnosis of porokeratosis of Mibelli There is a sharp border between the normal skin and the involved skin

DR. W R HUBLER I believe that vitamin A has been used in the treatment of porokeratosis of Mibelli with some success At the last meeting of the American Academy of Dermatology a patient with this disease was presented, and several dermatologists stated that they had noted improvement following administration of large doses of vitamin A

George W Binkley, M D, *President*
D N MacVicar, M D, *Secretary*
Sept 25, 1947

Acrosclerosis with Calcinosis Presented by DR CHARLES MARTIN JR (by invitation)

Poikiloderma Atrophicans Vasculare with Changes of Mycosis Fungoides, Basal Cell and Squamous Cell Epithelioma Presented by DR W MARMELZAT and DR A E WALKER (service of DR H N COLE and DR J R DRIVER)

A Case for Diagnosis (Parapsoriasis? Erythrodermie Congénitale Ichthyosiforme?) Presented by DR E W NETHERTON

A Case for Diagnosis (Tuberculosis Cutis?) Presented by DR G H CURTIS and DR E W NETHERTON

Steatocystoma Multiplex (Pringle) Presented by DR H N COLE and DR J R DRIVER

Epidermolysis Bullosa Presented by DR JOHN BONNER for DR C F MCKHANN (by invitation)

Keratosis Follicularis (Darier's Disease) Improvement After Therapy with Vitamin A Presented by DR E L GLICKSBERG

A Case for Diagnosis (Erythema Elevatum Diutinum? Eosinophilic Granuloma?) Presented by DR I L SCHONBERG

S F, a white man aged 62, first noted swellings on the head and the left arm in 1926 At that time he was treated with various methods, including roentgen irradiation and use of solid carbon dioxide After the application of the solid carbon dioxide an ulcerated area, which required many months to heal, developed on the scalp Since that time the patient has acquired new tumors on the left part of the chest and on the nose These have grown slowly and have darkened About three months ago several nodules were removed surgically from the left breast and the left arm The lesions have been asymptomatic

General physical examination showed essentially normal conditions On the front and the left side of the nose there are two nodules, one the size of a bean and the other the size of an almond The tumors are sharply demarcated, reddish brown and firm to palpation On the left arm there are two dollar-sized areas of atrophy, at the border of which there are pea-sized to bean-sized violaceous nodules There is an atrophic, circular scar, 6 cm in diameter, on the scalp

Treatment has consisted of irradiation with filtered roentgen rays, without results

The results of urinalysis were normal, as was the examination of the stools The hemogram revealed 5,200,000 red blood cells, 10,000 white cells, and 13 Gm of hemoglobin, with a differential count of 62 per cent polymorphonuclear cells, 38 per cent lymphocytes and no eosinophils Testing for allergic reactions gave negative results

A biopsy specimen taken from the wall of the chest showed in the dermis and underlying subcutaneous tissue a circumscribed nodule, measuring about 1 cm in long diameter The central portion of the nodule was composed of dense bundles of collagenous fibers, which were diffusely infiltrated by wandering cells Toward the periphery of the nodule the blood vessels were prominent and considerably increased in number and showed pronounced perivascular infiltration by wandering cells, among which eosinophils predominated The most characteristic changes appeared to be at the base of the lesion in the subcutaneous fat, with vessels thickened there, the media showed slight infiltration by eosinophils, and the regional stroma showed intense infiltration by wandering cells, among which eosinophils predominated

At one edge of the nodule in the dermis there were large bundles of smooth muscle, apparently hypertrophied smooth muscle of a tortuous artery The epidermis was thinner than average, and interpapillary projections were obliterated There was a moderate amount of brown granular pigment in the basal epithelial cells

A second biopsy specimen, taken from the arm, showed a similar picture, but with less advanced sclerosis of the central portion of the nodule than was seen in the material from the wall of the chest At the base of the lesion there was a thick-walled blood vessel In the lesion itself there are numerous blood vessels showing intense cellular infiltration of the vascular wall and perivascular tissue, in which eosinophils predominate

Section stained by the azocarmine method showed an increase in blue-stained fibrous tissue, especially in the lesion from the chest wall, and abundant red-stained smooth muscle bundles in the area, suggesting tortuous or aneurysmal blood vessels in the dermis

Monocytic Leukemia, Schilling Type, Nodular Cutaneous Lesions Presented by DR G M STROUD

A Case for Diagnosis (Melanosis? Poikiloderma of Civatte? Chloasma?) Presented by DR A E WALKER and DR W MARMELZAT (service of DR H N COLE and DR J R DRIVER)

Rosacea-like Tuberculid of Lewandowsky Presented by DR W R HUBLER

George W Binkley, M D, *President*
George H Curtis, M D, *Secretary*
Gerard A DeOreo, M D, *Reporter*
Oct 23 1947

Congenital Ichthyosiform Erythroderma, Persistent Notochord Presented by DR M H GUSTAFSON, DR E H JONES JR and DR M UTTERBACH (service of DR J E RAUSCHKOLB and DR G A DEOREO)

Nonspecific Dermatitis, Associated with Lymphoblastoma Presented by DR M H GUSTAFSON, DR E H JONES JR and DR M UTTERBACH (service DR ROY W SCOTT)

Lymphangiectasis of Vulva, Secondary to Probable Tuberculous Salpingitis, Pulmonary Tuberculosis, Moderately Advanced Presented by DR M H GUSTAFSON, DR E H JONES JR and DR M UTTERBACH (service of DR J E RAUSCHKOLB and DR G A DEOREO)

A S, a 29 year old woman, was first seen on the dermatologic service in September 1947, complaining of pruritic lesions of the vulva, of four months' duration She said that they had gradually increased in size and that the pruritus had become much more pronounced in the previous three weeks, with some weeping of the lesions She noted that a watery material was obtained from the individual lesions if she pricked them with a needle

Both the labia majora and the labia minora are covered with acuminate, cystic lesions, which are slightly tender and moderately pruritic The lesions are tense and are filled with a thin, colorless fluid Large, nonpigmented, polypoid lesions surround the external anal orifice Numerous healed scars are present on the abdomen and thighs The anal sphincter admits the index finger only, with much pain The rectum, within the reach of the examining finger, exhibits no abnormalities Bronchovesicular breath sounds, with fine, post-tussic rales, are heard at the apex of the right lung

Reactions to a skin test with old tuberculin (1 100,000) were positive Those to the Frei test were negative The Kline and Wassermann reactions of the blood were negative Results of urinalysis and the hemogram were within normal limits The roentgenogram of the chest revealed moderately advanced pulmonary tuberculosis of the upper lobe of the right lung

Histologic examination showed that the papillary projections of the epithelium were elongated and that there were many clusters of lymphocytes and plasma cells scattered throughout the underlying stroma, especially about the capillaries Just beneath the epithelium there were many dilated lymphatic spaces

MANHATTAN DERMATOLOGIC SOCIETY

David Bloom, M D, *Chairman*

Wilbert Sachs, M D, *Secretary*

March 11, 1947

Erythroplasia of Queyrat Cured. Presented by Dr E W Abramowitz

W L is a white man aged 42, born in the United States, married, with one child He works as a supervisor at a paper manufacturing company

He first came under my observation on Sept 20, 1945 He presented weeping, erythematous patches on the glans penis and the shaft Around this area there were numerous areas of telangiectasia said to have followed roentgenologic therapy to the affected areas, with no apparent effect on the original lesions The duration of the eruption was three and one-half years

He failed to respond to ordinary topical remedies such as Aloe vera pulp and ointment, penicillin or various soothing applications prescribed by other dermatologists and by me I finally resorted to a proprietary preparation containing menthol, phenol, camphor, oil of cloves, oil of eucalyptus and lime water in a vanishing cream base of undisclosed formula Since this has been used, the eruption has healed and the patient has had no further trouble The telangiectasia has remained His wife has recently given birth to another child

DISCUSSION

Dr Jack Wolf I think that this is an interesting and important case We have seen patients who have been cured, at least temporarily, with radiation, the improvement extending over several years Spontaneous remissions also probably occur in the course of the disease Apparently we do not as yet have the complete picture of the rationale of treatment or of the cure of erythroplasia of Queyrat

Dr Perry M Sachs (by invitation) I should like to know the time relationship between the roentgen treatments and the local therapy

Dr George C Andrews I accept the diagnosis in this case, but I think that generally we have to be cautious about accepting the diagnosis of erythroplasia I have in mind a patient whom I saw about two years ago He had had a penile eruption for about two months It was diagnosed as erythroplasia after biopsy by Army physicians On questioning him I found that he had taken sulfadiazine a month or so before the eruption began I told him that I would not accept the diagnosis of erythroplasia and gave him a mild lotion to use, and the balanitis cleared up entirely without any other treatment It is possible that the sulfonamide drugs produce eruptions something like erythroplasia at times We do not know what causes erythroplasia It may come from different things in different persons, so what cures one may not necessarily cure another When carcinoma is definitely present, it is a different matter The whole subject is rather involved

Dr Nathan Sobel These are interesting cases, and the condition is sometimes difficult to diagnose, as Dr Andrews and others have said When we see

The case of G S is of a condition I have never seen before, however Clinically, this looks like the male counterpart of an esthiomene, in which there is a urinary passage in the perineal area There are thickening and chronic inflammatory changes in the rectum and exuberant fibrotic growths on the penis and the pubic area The condition has improved tremendously in the last months from simply a little plastic surgery and the use of penicillin to clear up the secondary infection The Frei test, skin tests for chancroid and serologic tests gave negative reactions We found no smear positive for fusiform bacilli of Vincent Unfortunately, the smear for Donovan bodies was not made because the case was not into our service, although we recommended that it be done The disorder has probably resulted from a long-standing gonorrhea in which there was a posterior stricture and a false passage which opened in the perineum, with extravasation of urine into the structures adjacent to it, chronic inflammation of the structures and secondary infection being produced The diagnosis of granuloma telangiectaticum pyogenicum probably was made because there was an infected granuloma, although clinically the tumor is not the pyogenic type

Psoriasis Arthropathica Presented by Dr M H Gustafson, Dr E H Jones Jr and Dr M Utterbach (service of Dr Roy W Scott)

Morphea or Lichen Sclerosus et Atrophicus(?) Presented by Dr M H Gustafson, Dr E H Jones Jr and Dr M Utterbach (service of Dr J E Rauschkolb and Dr G A DeOreo)

Multiple Benign Cystic Epithelioma, Alopecia Areata Presented by Dr M H Gustafson, Dr E H Jones Jr and Dr M Utterbach (service of Dr J E Rauschkolb and Dr G A DeOreo)

H D, a 44 year old woman, has four siblings, her mother and a sister have lesions similar to hers The patient has a daughter, aged 23, who is just beginning to exhibit similar lesions

Acrokeratosis Verruciformis Presented by Dr M H Gustafson, Dr E H Jones Jr and Dr M Utterbach (service of Dr J E Rauschkolb and Dr G A DeOreo)

W H, a 16 year old girl, was first seen in the dermatologic service in June 1947, with lesions on the hands and feet, which have been present since birth They have produced no symptoms and have not changed in size since puberty

The patient's aunt and father have had similar lesions since birth The patient was treated with penicillin therapy for secondary syphilis, ending Sept 19, 1947 She was hospitalized for acute and chronic pelvic inflammatory disease in 1946 She states that her parents are not related by blood

Over the proximal interphalangeal joints and the knuckles of both hands are multiple, firm, keratotic papules, measuring 2 to 8 mm in diameter Over the medial and lateral aspects of both palms and soles and the tendo achillis are multiple, small, discrete, firm papules

The roentgenogram of the chest showed normal conditions The results of urinalysis and the hemogram were normal The Kline and the Wassermann reactions of the blood were 4 plus, with a titer of 1 64

DISCUSSION

DR NATHAN SOBEL It is an excellent result

DR JACK WOLF I think that Dr Sachs is to be congratulated It is the first opportunity that we have had of seeing any of the patients whom he has been treating We must take cognizance of the fact that this is not the only case he has shown tonight in which he has obtained a good result but that he is reporting a series of 10 cases, all of which he has followed assiduously Dr Abramowitz' case, which was reported tonight, and the instances of spontaneous improvement that we have seen do not detract in any way from the excellent work which Dr Sachs has done It adds an excellent method of treatment for a disease with which we have had so much trouble

DR MAX SCHEER I wonder whether the patients whom we have seen in this country with the disease which we label erythroplasia are suffering from what the French call erythroplasia According to the French authors, it is not only a precancerosis but it is a cancerosis and it invariably ends with metastasis to the inguinal lymph nodes and death In fact, there have been reports of cases in which the first lesion was a malignant process of the lymph node, followed later on by the erythroplasia of the glans penis In view of the fact that all the French cases have resulted in cancer unless radical treatment was performed and in view of the fact that, according to Dr Sachs, cancer has not developed in a single one of our patients, I wonder whether we are dealing with the same disease or whether it is contact dermatitis or some other kind of dermatitis, as Dr Rosen has suggested

DR PERRY M SACHS (by invitation) Whether or not we are dealing with the erythroplasia described by Queyrat is of secondary import It is erythroplasia as seen and diagnosed by dermatologists in this country and a disease which has proved resistant to all forms of therapy short of heroic measures

DR DAVID BLOOM I should like to ask Dr Sachs how he came to think of this treatment?

DR JACK WOLF Regardless of whether or not we are dealing with the disease which the French authors described, it must be admitted that if Dr Sachs has had such excellent results in the type of disease we see and which we call erythroplasia it is an important contribution to the therapy of a troublesome and obstinate disease We should be able to decide in the near future whether it is the same disease as that described by Queyrat

DR GEORGE C ANDREWS I had 1 case of erythroplasia, clinically typical and diagnosed microscopically by Dr Machacek, in which epithelioma of the penis developed and the patient died of metastasis

DR GEORGE M LEWIS Dr Sachs has observed 10 cases, which is probably 9 more than Queyrat had Why should we necessarily perpetuate Queyrat's conception unless it is the same as ours? I would support Dr Sachs's opinion over that of any of the foreign observers His cases are those in which we are interested It may be a different disease from the one described abroad, but it is the one that we see Furthermore, I think his treatment has been effective, and until this time our treatment has been poor Dr Sachs deserves a great deal of credit, obviously, he has controlled his work and has tried a great many remedies It is not something he thought of last week—he has been at it for a long time I think it is good work, he has not found the cause, but that is not always essential There are many diseases in which treatment is effective although the cause is unknown

reactions to the serologic test for syphilis Numerous lumbar punctures have shown no abnormalities

His blood pressure is 154 systolic and 110 diastolic Examination of the genitalia reveals a 2 by 3 cm ulcer on the left side of the dorsal surface of the glans penis, extending down to the shaft The ulcer has a red, granulating base, partially covered by a thick, dry crust, and the edges of the ulcer are slightly thickened and rolled The lymph nodes are not remarkable

In June 1946 the reaction to the Kahn test was 4 plus, with 10 Kahn units, and reactions to the complement fixation test were negative, however, on two occasions in November the serologic reactions were negative Several urinalyses have shown a specific gravity from 1 010 to 1 022, and on several occasions there have been white blood cells with clumping Biopsy of the penile lesion showed acute inflammation of the skin, with ulceration and atypical hyperplasia of the epithelium An electrocardiogram showed an essentially normal record, with slight elevation of the S-T segment

A Frei test gave negative reactions, and no definite inclusion bodies were seen on the slide of the biopsy specimen The patient has concluded a course of streptomycin, consisting of 4 Gm a day for six days The only other medication has been warm saline compresses to the penile lesion On this therapy there has been definite healing at the periphery of the ulcer and the ulcer is now approximately 1 cm smaller in diameter

The following is the report of the microscopic examination "Examination revealed that the epithelium was ulcerated The ulcer was densely infiltrated with many lymphocytes and plasma cells Over the ulcer there were necrotic debris and many polymorphonuclear leukocytes There were islands of epithelial cells in which the nuclei were large and vesicular, and there were a few large, irregular, oval bodies, resembling somewhat a molluscum body Some of the epithelial cells showed metallic diversion The diagnosis was acute inflammation of the skin, with ulceration and atypical hyperplasia of the epithelium"

DISCUSSION

DR G A DEOREO I think that this man has granuloma inguinale The rapid improvement on treatment with a relatively short course of streptomycin also points toward this diagnosis It is true that there are certain findings in the biopsy which suggest pseudoepitheliomatous hyperplasia, but these changes are frequently seen in granuloma inguinale

DR J E RAUSCHKOLB The chronicity of the lesion, the lack of pain and the resistance of the disorder to ordinary antisyphilitic drugs point, as Dr DeOreo says, to pseudoepitheliomatous hyperplasia, but the condition is not neoplastic in character, and it cannot be anything else but granuloma inguinale One ought to be able to find Donovan bodies, however

DR H N COLE This is a very interesting case One hesitates to make two diagnoses if one will suffice I have seen sections from a large number of cases of granuloma inguinale, and I have seen several examples of pseudoepitheliomatous hyperplasia, but I have never observed anything like the condition this man presents, as seen in the section I do not see how one can avoid calling this disorder intraepithelial carcinoma as well as granuloma inguinale Of course, in Negroes one does not very often see epitheliomatous changes on the skin, but this section shows such a remarkable picture that I do not see how we can refuse to make that diagnosis It would be interesting to have another report on this patient later

region of the hypochondria and the under surfaces of the breasts showed a definite picture of poikiloderma, consisting of reticulated pigmentation, telangiectasia and atrophy There was decided wrinkling of the upper parts of the breasts and reticulated hyperpigmentation and atrophy in both axillas The lower part of the back, inner aspect of the upper extremities and back of the neck were scaly and erythematous The axillary lymph glands were enlarged The upper eyelids showed erythema and edema, which had been present for the past two months

Laboratory examinations, including urinalysis, serologic tests of the blood for syphilis and complete and differential blood counts, gave essentially normal results

Biopsies of material taken from the skin under the breast and from the thigh showed features of poikiloderma

DISCUSSION

Dr Nathan Sobel The patient definitely had poikiloderma in the areas over the lower part of the breasts and atrophy over extensive areas elsewhere, but I am puzzled by the hyperkeratosis of the palms and soles and do not believe that is often found in cases of poikiloderma

Dr E W Abramowitz I have the same difficulty in reconciling the hyperkeratosis of the palms and soles I do not recall having seen it in cases of poikiloderma It is a question whether some other disease should be considered or whether further observation is necessary before the case is labeled poikiloderma

Dr George C Andrews The case reminded me of the cases of dyspituitarism with poikiloderma-like changes, reported by Bruno Bloch I think that the woman has endocrine disease A basal metabolism test, roentgenograms of the sella turcica, an encephalogram and various other tests are indicated In many cases of Cushing's basophilism the disease is related not to the pituitary but to the adrenal glands, so this case should be studied from that angle I am wondering whether the hyperkeratosis of the soles could be related to localized myxedema in which there is a great deal of lymph stasis that produces verrucous changes

Dr E W Abramowitz Dr Andrews brought up a point which might still point to the pituitary The patient may have keratoderma climactericum

Dr Fred Wise I agree with those who believe that the eruption is caused by a polyglandular disturbance similar to Cushing's syndrome, in which almost invariably telangiectasia and pigmentation of the lower portion of the breasts are present Poikiloderma is merely a symptom, whereas poikiloderma vasculare atrophicans is a definite clinical entity, as described by Jacobi This patient has a poikilodermatous skin associated with polyglandular disturbances, but the condition should not be described as a case of Jacobi's disease because, as the name suggests, that has a variegated appearance It would be better to describe it under a name which at least suggests pituitary basophilism or Cushing's syndrome

Dr David Bloom I realize the difficulty in diagnosing this condition Besides the poikiloderma-like eruption and the scaly plaques, the patient shows extensive keratosis of the palms and soles, which would fit in with psoriasis or keratoderma climactericum One finds erythema of the eyelids in poikilodermatomyositis, but in this patient it developed only one month ago, late in the course of the disease I am inclined to agree with Dr Andrews and Dr Wise in regard to a thorough study of the patient in order to eliminate an endocrine condition such as Cushing's pituitary basophilism A definite diagnosis, of course, cannot be made at present

A Case for Diagnosis (Leukonychia and Hyperpigmentation of Gums and Lips) Presented by Dr E W Abramowitz

DISCUSSION

DR G H CURTIS Clinically, the disease looked like sarcoidosis

DR B LEVINE I saw this man some years ago, and I thought at that time that he had sarcoidosis Many other dermatologists have seen him since

DR G A DEORDO In the 2 cases of erythema elevatum diutinum that I have seen, the edges of the lesions were more perpendicular than they are in this case and the surface formed a plateau The color was not quite as intense as in this case, and the microscopic picture was considerably different from the one we see in this case I should like to suggest the possibility of Kaposi's hemorrhagic disease

DR B PERSKY I should not quite agree with the diagnosis of eosinophilic granuloma here because of the absence of large cells either in the skin or in the bone There were quite a few eosinophils, but I do not think they would add up to the number seen in eosinophilic granuloma I have had occasion to deal with a case of erythema elevatum diutinum, with the characteristic features This case showed ring-shaped lesions around the digits and around the joints, quite blue but not as deeply blue as the lesions in the present case The lesions here somewhat resembled granuloma in that they had a smooth surface and an annular configuration They did not show the picture of granuloma annulare histologically There is one other possibility which I should like to suggest I am not at all sure how accurate the history is I should like to suggest the possibility of periarteritis nodosa There were some vascular changes I think that more biopsies might reveal those features, and possibly further observation and a fuller history as to whether there were remissions or relapses might help

DR I L SCHONBERG When I saw this patient for the first time I was very confused, as you might expect, and on going over his history there were several things that I thought of I was hoping that when I made the biopsy the diagnosis would be sarcoid, but unfortunately it could not be made on the section However, there was a new lesion at the base of the left breast, and we also decided to take a border specimen from the lesion of the left arm On pathologic examination, the condition was reported as periarteritis nodosa I do not feel that the disorder falls in that class, at least clinically On reading the literature, I became more and more confused as to whether or not it fitted in with that diagnosis In the February 1947 issue of ARCHIVES, pages 155 to 201, there are three or four articles on erythema elevatum diutinum and eosinophilic granuloma The examination of the section did not reveal a picture fitting into the type of erythema elevatum diutinum as described by the first author, but observations did fit in with the picture described by Weidman He stated that erythema elevatum diutinum presents a polyarteritis with a cellular infiltrate He quoted an Italian dermatologist, who described a case almost identical with the one I have shown He described lesions on the extensor surface of the hands, the ears, the face and the buttocks According to some of the descriptions, many of these cases began in early life However, there was a group of cases in persons usually over 40 years of age, who presented similar lesions Two types were described the "Hutchinson type," or soft type, with soft plaques, and the "Bury type," with hard nodules which undergo a purplish discoloration There is also a third type, which resolves by itself It is rather difficult to classify this case, but I do feel that there are some indications that it fits into one group or the other

A Case for Diagnosis (Lymphatic Leukemia Following Vaccination Against Smallpox?) Presented by DR DAVID BLOOM

J H, a man aged 80, was referred to me in September 1947 by Dr H Wolf because of a tumor which had developed in the area of smallpox vaccination five months previously The patient also suffers from generalized pruritus

On the external aspect of the right arm there was a walnut-sized, erythematous, raised and indurated, globular tumor, firm in consistency and with borders infiltrating the surrounding skin in an ill defined manner In the vicinity of the tumor there were a number of erythematous, pea-sized and excoriated papules In addition to this lesion which caused severe pruritus, there were excoriated lesions on the forearms, the lumbosacral region and the legs In the axillas slightly enlarged nodes were palpable

Biopsy of the tumor on the arm revealed a "nonspecific type of granuloma" A blood count on two occasions showed a normal red cell count, but a white cell count of 13,600 on one occasion and 16,900 on another The differential count, in addition to 3 per cent blasts, showed 58 per cent lymphocytes and 35 per cent polymorphonuclear leukocytes and on another occasion 76 per cent lymphocytes

The patient is in good general health except for the generalized pruritus which disturbs his sleep The lesion on the right arm has diminished in size after several treatments with filtered roentgen rays

DISCUSSION

DR WILBERT SACHS The microscopic section that I examined was from the arm and suggested a nonspecific granuloma The characteristic picture of lymphatic leukemia, which undoubtedly should be present in a lesion of this size, was not seen If the patient has lymphatic leukemia, it is unrelated to the lesion on the arm

DR SAMUEL M PECK A number of years ago I thought that it would be interesting to take cases of chronic lymphatic leukemia, acute leukemia and diseases like purpura hemorrhagica and do trichophytin, tuberculin and venom tests and study the histologic appearance, to see how a known blood picture would influence a histologic reaction with which I was familiar I found nothing very striking

DR WILBERT SACHS Instead of a leukemia infiltration, one finds a leukemid type of reaction, and this is nonspecific

DR ANTHONY C CIPOLLARO Does the patient have leukemia in the first place, and did vaccination have anything to do with it if he has? There has not been enough evidence to indicate a relation between smallpox vaccination and leukemia

DR DAVID BLOOM The diagnosis of leukemia was suggested by the increase in the white blood cells, the high lymphocyte count and the presence of blasts This opinion was shared by the hematologist, who advised sternal puncture In spite of the absence of a confirmatory histologic report, this diagnosis is most probably correct

Acrodermatitis Pustulosa Perstans Presented by DR WILBERT SACHS

Lymphoblastoma, Clinically Poikiloderma, Histologically Mycosis Fungoides Presented by DR JACK WOLF

a patient apparently cured, we are inclined to question the diagnosis I think we must accept the fact that this patient has had erythroplasia and try to give credit where it is due

DR E W ABRAMOWITZ I am sure that Dr Sachs will bring out other important features of this disease Erythroplasia was always considered a serious disease, a precancerosis Radical measures, even including amputation, were discussed I do not recall ever seeing a patient with erythroplasia of the penis in whom cancer of the penis developed I have wondered, therefore, whether radical measures were justified In this case, roentgen rays apparently had no effect except to produce telangiectasia I tried to treat this telangiectasia because in the beginning it seemed to bother the patient He was able to tolerate mild applications of solid carbon dioxide to the telangiectatic area I soon stopped that, however, and used mild boric acid ointment and solution, Aloe vera pulp and then ointment, with little improvement *It was not until Dr Cipollaro showed* a patient with erythroplasia who had responded to this proprietary preparation that I told my patient about it and suggested its use The patient reported immediate relief I think one can say now that this lesion is healed There has been no activity for several months

I should like to mention another patient, brought to me by a urologist who was considering the possibility of radical measures, there was an erosive lesion of the penis which he thought was cancer I thought it was a drug eruption, as the lesion was typical of a fixed eruption I questioned the man about phenolphthalein, and he denied taking it I was so convinced that he was lying that I went to his house and found feen-a-mint® (laxative containing phenolphthalein) packages and wrappers When he stopped using this the ulcerations disappeared It is not unusual to see lesions in the mouth and on the penis from phenolphthalein, and I have seen a fixed eruption on the penis and in the mouth from veronal® (barbital U S P) and other barbiturates

Erythroplasia—Cured Presented by DR WILBERT SACHS

E G K, a white man aged 45, first noticed a small red papule on the glans penis two and one-half years ago This grew until almost the entire glans was involved There was continuous oozing and slight itching The patient had been treated by several competent dermatologists, all of whom had made a diagnosis of erythroplasia Therapy consisted of local applications of various preparations and the use of roentgen rays, radium and hormone injections, with little or no results

Laboratory examinations, including blood counts, urinalysis and serologic tests, revealed no significant findings Microscopic examination confirmed the diagnosis of erythroplasia

When first seen by us in December 1946, the patient had an erythematous, shiny, oozing patch over most of the glans penis There was no scaling or crusting and no induration The following medication was applied locally, twice a week, for three weeks 0 3 Gm of neoarsphenamine dissolved in 4 cc of distilled water, to which 1 cc of glycerin is added

Oozing and all subjective symptoms disappeared within one week The lesion became crusted, and in the following few weeks the entire process disappeared, leaving no sequelae

DR WILBERT SACHS I should consider other possibilities in preference to granuloma annulare Before accepting this diagnosis, I should like to study the microscopic sections Although numerous giant cells may be found as a rule they are not a feature of granuloma annulare

DISCUSSION

DR THOMAS N GRAHAM I think that the individual papules on the dorsum of the right hand look like the lesions usually observed in granuloma annulare, although they are not in annular formation However, the lesions on the forearm do not resemble that dermatosis clinically but, rather, suggest lichen planus

DR FRANK E CORMIA (by invitation) Dr Peck and I had the same opinion—that, clinically at least, the lesions are suggestive of amyloidosis

DR SAMUEL M PECK What struck me was the two distinct types of lesions The first was the skin-colored lesions on the back of the hands and even on the elbows which I should not hesitate to call granuloma annulare Then I saw another type, peculiar brownish-bluish lesions which made me think of amyloid disease but the fact that the microscopic appearance of three lesions was the same makes me doubt that we are dealing with amyloidosis The peculiar cases shown at the meeting of the American Academy of Dermatology and Syphilology in Chicago turned out to be extracellular cholesterosis I should certainly like to see studies made along that line

DR ISADORE ROSEN The clinical features suggest the lichenoid type of sarcoid rather than granuloma annulare

DR NATHAN SOBEL One of the thoughts that first occurred to me was possible amyloidosis, but against that is the complete absence of itching, which is certainly a distinctive feature of amyloidosis The lesions around the anterior surface of the wrist are skin colored and hard and could fit into the picture of granuloma annulare The other lesions are not characteristic and look almost like lichen planus at a casual glance I think it best to include all the lesions as granuloma annulare

DR MAURICE J COSTELLO This case impressed me also as one of lichenoid sarcoid I should like to see the results of tuberculin tests and roentgen examination of the chest I think that it is true that granuloma annulare responds to roentgen rays

DR DAVID BLOOM The biopsy report was surprising to all of us who had observed this case and did not think of the diagnosis of granuloma annulare Although I have seen atypical cases on several occasions, particularly of disseminated granuloma annulare in children, I have never seen a case similar to this one The patient will be studied more thoroughly

Darier's Disease Presented by DR NATHAN SOBEL

A Case for Diagnosis (Keratoses? Lupus Erythematosus?) Presented by DR ANTHONY C CIPOLLARO

Mycosis Fungoides Presented by DR MAX SCHEER

Parapsoriasis Guttata Presented by DR MAX SCHEER

Hypersensitivity to Cinnabar in a Tattoo Presented by DR JACK WOLF

Multiple Superficial Basal Cell Epithelioma with Arsenical Keratoses Presented by DR JACK WOLF

DR JACK WOLF Dr Sachs says that his therapy produces an adherent crust which remains for a long time Does he think, then, that we can achieve more rapidly the same type of crust and destruction by desiccation with the high frequency current or by the use of acids such as trichloroacetic acid? Is there any essential difference?

DR FRED WISE I am in complete accord with what Dr Lewis has said, but I think it would be not only desirable but necessary for the author to state that he is not sure he is dealing with the identical disease described by Queyrat American readers regard the term erythroplasia as meaning erythroplasia of Queyrat, and I suggest a notation to the effect that Dr Sachs is not sure he is dealing with that entity but that he is dealing with a disease similar in appearance and in chronicity, which, however, does not eventuate in cancer

DR DAVID BLOOM Neoarsphenamine dissolved in distilled water and then in glycerin, in 10 per cent concentration, has been used for several decades in the treatment of Vincent's infection of the mouth It is logical to assume that the beneficial effect obtained by Dr Sachs in his cases of erythroplasia is due to the effect on spirochetes or bacteria In these cases, therefore, there should be bacteriologic examination, irrespective of their duration

DR GEORGE M LEWIS I wonder if some of the malignant processes that supervene in these cases are the result of the treatment administered, such as desiccation or the use of pastes and irritant remedies In your opinion, Dr Sachs, is treatment ever responsible for malignant changes?

DR WILBERT SACHS The disease treated in this case, and in the other 9 cases reported in our paper, is the same as that described by Queyrat The French authors believe that in most of the cases the lesions become malignant The experience in our cases is not in accord with this view There have been only 2 cases reported in the American literature in which malignant changes developed In 1 the original diagnosis was questioned, in the other, the lesion was basal cell epithelioma and not erythroplasia Dr Andrews' case would make a third There are cases in which the lesion has all the clinical features of erythroplasia but microscopically proves to be either basal cell epithelioma or Bowen's disease However, as Dr Lewis suggests, it is always possible for a malignant process to follow long-continued treatment which includes such heroic measures as those employed in an endeavor to control erythroplasia In reply to Dr Wolf's question, desiccation and escharotic preparations have produced good results in some cases, but with sequelae and disfigurement These have not followed the treatment we are reporting

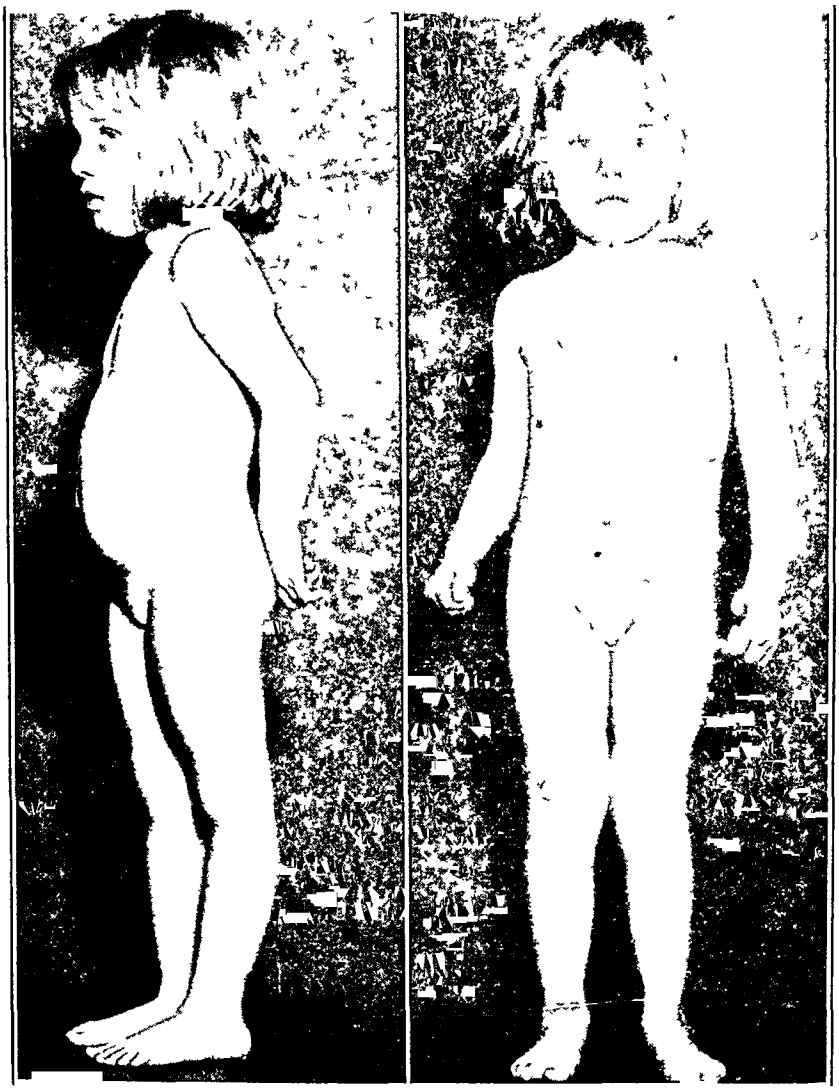
A Case for Diagnosis (Poikiloderma Atrophicans Vasculare?) Presented by DR DAVID BLOOM

R C, a white woman aged 47, complained of an eruption on the palms and soles of eight months' duration and of a generalized eruption of five months' duration The family history and the past history was essentially irrelevant The patient seems to be in fairly good general health

The plantar surfaces of the feet, and particularly of the heels, showed pronounced hyperkeratosis The dorsal surfaces of the feet and toes were slightly scaly and mildly erythematous The palms were dry and scaly and showed accentuation of the natural lines The backs of the hands and fingers were similarly affected, but to a lower degree The anterior and lateral aspects of the thighs and hips showed erythema, scaling, wrinkling and mottled hyperpigmentation The

DR JOHN G DOWNING I rubbed my finger nail on the leg After a few minutes a wheal appeared I think that it is a case of urticaria pigmentosa Whether this lesion belongs to the nevoid group, I do not know, other cases of urticaria pigmentosa are so classified

DR BERNARD APPEL, Lynn, Mass The histologic examination should have revealed a typical infiltrate if this were urticaria pigmentosa



Pigmented lesions in a 4 year old girl

Multiple Epidermal Cysts of the Skin Presented by DR MAURICE M TOLMAN, Boston

A 29 year old white nurse, S C, is presented with lesions on the back of her hands of six months' duration She first noted dermatitis venenata on the knuckles of both hands from handling a patient's flowers This was an acute vesicular eruption which healed with mild therapy but left behind small white nodular lesions Four months ago she received roentgen therapy, 500 r in divided doses This caused increased redness and tenderness, there was no improvement in the nodular lesions In the last few weeks they have become somewhat less prominent without further therapy

Maurice J Costello, M D, *President*

Wilbert Sachs, M D, *Secretary*

Oct 14, 1947

Generalized Progressive Scleroderma and Dermatomyositis Improved with Diphenhydramine (Benadryl®) Presented by DR MAURICE J COSTELLO

J F, a married woman aged 42, was presented before this Society on Oct 10, 1944, with a generalized progressive scleroderma and dermatomyositis associated with acrosclerosis and Raynaud's phenomenon

Since March 1946 she has been given 400 mg of diphenhydramine daily, with remarkable improvement, there is increased mobility of the joints and softening of the boardlike infiltrations and the dyspnea, wheezing, dysphagia and loss of muscle power have been relieved to a remarkable extent The results have been so spectacular that the only abnormality remaining is the irreversible contraction of the fourth and fifth fingers

DISCUSSION

DR DAVID BLOOM I believe that diphenhydramine in such large doses should be given to a patient only when he is hospitalized and under close observation I saw a patient who had received 150 mg of the drug daily over a period of several weeks suddenly collapse with a sensation of constriction in the chest and numbness of the upper extremities

DR MAURICE J COSTELLO The patient's condition was so advanced that she had not only severe edematous thickening of the skin and lack of mobility of the joints but also dysphagia and dyspnea Her general practitioner gave her diphenhydramine mainly to relieve what he considered asthmatic symptoms, and she has taken 400 mg every day for a year and a half I presented this patient before this society in 1944, and the change since has been nothing short of remarkable This patient had received dihydrotachysterol (hytacherol®) with no benefit

DR SAMUEL M PECK When dihydrotachysterol works, it is only on the edematous part If diphenhydramine works, it is something entirely different I think that I shall try iontophoresis with pyribenzamine,® as I am doing with neurodermatitis, especially of the hands I know that the drug stays in the tissues for weeks

DR ANTHONY C CIPOLLARO Does diphenhydramine produce vasodilatation?

DR MAURICE J COSTELLO I believe so, because the patient has been free of the blanching of the fingers associated with Raynaud's phenomena I might add that the only other case I have seen recently that approaches this in therapeutic result was that of a patient whom I sent from Lenox Hill Hospital to Bellevue Hospital, who received a high protein diet with large doses of a protein hydrolysate (amigen®) Graphic studies were taken of the improved mobility of the joints and the skin overlying them

DR SAMUEL M PECK Was there a reversal of result with primary lesions again with a violet ring?

DR MAURICE J COSTELLO No I have never seen improvement from dihydrotachysterol that was permanent The diphenhydramine was discontinued in this case for three weeks, with recurrence of symptoms

eruption until the oil that caused the dermatitis was carried by the effervescent soda water to her face Wiley Sams (ARCH DERMAT & SYPH **44** 571, 1941) reported a case of dermatitis based on the photodynamic action of lime oil

DR JOHN G DOWNING This patient has used nose drops which may have contained silver nitrate Silver nitrate is precipitated rapidly by sun I have seen cases in Florida similar to these after exposure to the sun

DR JOSEPH GOODMAN The patient used a silver salt eighteen years ago for gonorrhea

DR WALTER F LEVER The histologic sections show no evidence of argyria If the pronounced darkening of this patient's skin were due to argyria, one should be able to see silver granules in the sections even without resort to dark field illumination There is considerable increase of melanin in the basal layer and an abundance of melanin-laden chromatophores in the upper part of the corium I regard this case, from the histologic point of view, as one of hyperpigmentation

DR JOHN G DOWNING These patients always exhibit pronounced pigmentation if they are exposed to excessive sunlight Argyria will increase this tendency

DR WILLIAM R HILL I was not impressed with the possibility of argyria, although I did not examine the patient's nails and conjunctivas I agree with Dr Lever histologically, there was too much pigment to suggest argyria Such pigment is found around the sweat glands

DR BERNARD APPEL, Lynn, Mass I was impressed not only by the streak across the forehead that resembled hat band dermatitis but also by the discoloration of the face and neck Melanosis of Riehl should be considered In questioning this man about his diet, I found that he practically never ate any fresh vegetables or fruits I think that there is a possibility of this being the dietary deficiency type of pigmentation which Riehl originally described This is also consistent with the microscopic picture

DR G MARSHALL CRAWFORD By common usage, I think that the term Berlock dermatitis has come to represent almost any bizarre pigmentary deposit caused by photosensitizing agents on the skin It is difficult to see how such a sharply defined rectangular patch could be created without a pattern contact such as a hat band The dye therein, or tanning chemicals, might be incriminated

A Case for Diagnosis (Bacterid?) Presented by DR JOSEPH GOODMAN, Boston

Mycosis Fungoides in a 56 Year Old Woman Presented by DR MAURICE M TOLMAN, Boston

Mycosis Fungoides in a 46 Year Old Man Presented by DR MILDRED L RYAN, Brockton, Mass

DISCUSSION OF CASES OF MYCOSIS FUNGOIDES

DR MAURICE J STRAUSS, New Haven, Conn The woman has changes on her tongue Dr McCarthy pointed them out and said that they were lesions of mycosis fungoides, he had seen a similar case I have never before observed this and wonder whether it would be possible to have a biopsy done to prove it

DR FRANCIS P MCCARTHY Textbooks on dermatology and oral medicine show plates of tongue lesions in mycosis fungoides About twenty years ago I saw a tongue which presented lesions of mycosis fungoides, somewhat like those on this woman's tongue The lesions were raised and nodular, the largest was 0 5 by

A Case for Diagnosis (Lichen Planus? Psoriasis?) Presented by DR NATHAN SOBEL

G F, a woman aged 52, was first seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Oct 16, 1947 with an eruption of six weeks' duration

On the right upper eyelid there is a well defined, oval plaque which shows an erythematous, raised border and depressed, crusted center On the buccal mucosa there are divided plaques with reddish borders The entire scalp shows thickening of the skin, erythema and scaling There are erythematous, superficial, slightly scaly, well defined round plaques on the chest and on the upper part of the back and arms on the left On the extensor aspect of the thighs and inner aspect of the right thigh there are some purplish lichenified plaques There are erythema and fissuring in the genitocrural creases All the finger nails show onycholysis The nails of both big toes are greatly discolored, thickened and loose

The only laboratory report available to date is on the Wassermann reaction of the blood, which was negative

DISCUSSION

DR DAVID BLOOM The patient presents lesions on the lower extremities and on the buccal mucosa which look like lichen planus and an eruption of the scalp and changes in the nails suggesting psoriasis This combination of psoriasis and lichen planus has been reported on several occasions

DR NATHAN SOBEL I think that the lesion on the left buccal mucosa is probably a bullous lesion of lichen planus I have also previously seen lichen planus on the scalp To settle the question, biopsy would be necessary I think the changes in the nails are psoriatic

NOTE—It was reported at the succeeding meeting, in November, that biopsies, one from the leg and another from the neck adjacent to the scalp, both showed mycosis fungoides

A Case for Diagnosis (Peculiar Eruption of Granuloma Annulare?) Presented by DR DAVID BLOOM

M McH, a woman aged 41, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in October 1947, complaining of an eruption of one year's duration The eruption started first on the elbows, later it appeared on the lower extremities, and in the past three months it has involved the wrists There are no subjective symptoms

On the posterior and internal aspects of both lower extremities, extending as far as the middle of the legs, there is a profuse eruption of bluish-brownish, flat lesions, from the size of a lentil to that of a pea, some of which feel somewhat infiltrated A similar but less profuse eruption is seen on the flexor and internal aspects of both upper extremities Over both knees and elbows there are pink to skin-colored, raised, indurated papules Similar lesions are seen over the external malleolus of the left leg There are a moderate number of raised, dark red, firm, globular and elongated lesions on the flexor aspect of both wrists, extending to the forearm Over the sacrum, similar lesions form an irregularly shaped plaque

Microscopic examination of lesions from the wrist, elbow and thigh all showed the structure of granuloma annulare As reported by Dr Charles F Sims, the epidermis was thin, and the corium beneath showed basophilic degeneration In the upper and middle parts of the cutis were areas of granular degeneration surrounded by small, round and wandering connective tissue cells, epithelioid and giant cells The infiltrate took an arciform arrangement in many areas

noted these lesions on both her thighs and her legs Those on the thighs have gradually cleared, but lesions have persisted on the calves She stated that she bruises too easily but gives no history of epistaxis It was stated that some lesions bled on several occasions following minor trauma This woman was extremely nervous and suffered from melancholia during her only pregnancy five years ago, she has taken sedatives at night since that time There has been considerable menstrual irregularity The general medical history was otherwise noncontributory There was no history of similar lesions or of epistaxis in the family

Examination revealed a profusion of dilated blood vessels restricted to the lower third of each calf Most of these are of telangiectatic caliber but some are slightly larger They gradually fade out on the middle portion of the calves and on the sides of the legs

The prothrombin time (clotting time) of the blood plasma was found to be 20 seconds The sedimentation rate of the blood was 3 mm in 1 hour The cellular elements of the blood were normal A specimen removed for histologic examination revealed only atrophy of the epidermis and fibrosis of the corium One small area was treated by electrodesiccation with some resultant diminution in telangiectasia

DISCUSSION

DR WALTER F LEVER This disorder is really not too rare It was first described in the American literature by Stokes (*Am J M Sc* **149** 669, 1915) under the name of generalized telangiectasia and was thought to be associated with syphilis Among subsequently reported cases some patients had syphilis, but in most instances they did not It was also found that the disorder was not necessarily generalized, in patients with localized distribution the lower legs are most commonly affected The telangiectatic vessels are dilated venules They are dilated because their innervation is defunct Recently, in a patient with telangiectasia of the lower legs, I injected both a vasoconstricting and a vasodilatory drug intradermally, following Perutz' directions (*Arch f Dermat u Syph* **148** 313, 1924-1925) Intradermal injection of 0 1 cc of a 10 per cent solution of caffeine sodium benzoate caused the skin around the site of injection to become bright red, but the affected vessels did not change their size Similarly, 0 1 cc of a 1 1,000,000 solution of epinephrine injected intradermally caused blanching of the skin around the site of injection, but did not affect the telangiectatic vessels The disorder is harmless as such, but it is advisable to examine such patients for syphilis

Lichen Striatus in a 4 Year Old Girl Presented by DR G MARSHALL CRAWFORD and (by invitation) DR J H COX, Boston

Bernard Appel, M D, *President*

G Marshall Crawford, M D, *Secretary*

April 9, 1947

Psoriasis (Mycosis Fungoides?) Presented by DR JACOB H SWARTZ, Boston

Keratoses, Due to Arsenic, Taken for Psoriasis Presented by DR EDWARD A LAFRENIERE, Arlington, Mass

DISCUSSION

DR F RONCHESE, Providence, R I I wonder whether anybody here has treated keratoses with ozonides This treatment was reported by Sharlit (New

NEW ENGLAND DERMATOLOGICAL SOCIETY

Bernard Appel, M D, President

G Marshall Crawford, M D, Secretary

Boston, Feb 12, 1947

Incontinentia Pigmenti Presented by DR G MARSHALL CRAWFORD, Boston, and DR C R DAMIANI, Worcester, Mass

A 4 year old white girl of American birth, P W, is presented with an eruption on the trunk and upper part of the thighs present since early infancy At about the age of 3 months, pigmented streaks were seen on the back of the upper part of the thighs These gradually became more pronounced and extended upward, eventually involving the back and abdomen A year ago, when the patient had measles, the pigmented areas were observed to become scarlet, after recovery the areas gradually returned to the previous shade of brown No other member of the family has been affected by any similar condition There was no history of congenital anomalies, the child had a normal developmental history and was mentally alert

Examination reveals a pigmentary disturbance approximating the "bathing suit" distribution The upper limits are the xiphoid level anteriorly, the axillas laterally and the inferior edges of the scapulas on the back It extends downward over the trunk and across the hips and buttocks to about the junction of the upper and middle thirds of the thighs The lesions consist of symmetrically arranged striate and whorl-like pigmentary deposits of medium brown The majority of them are linear, and their length varies from 1 to 3 cm, most lesions are from 3 to 5 mm in width They are arranged in parallel fashion corresponding roughly to the cleavage lines of the metameric segments

A biopsy was performed, and histologic observations were reported as "consistent with lentigo"

DISCUSSION

DR WALTER F LEVER The histologic picture bears out the diagnosis of incontinentia pigmenti Considerable amounts of melanin were present in the upper part of the corium, whereas melanin in the basal layer was not increased Other forms of hyperpigmentation usually show increased pigmentation both in the basal layer and in the upper part of the corium

DR WILLIAM R HILL I think that Sulzberger and Bloch reported a case of incontinentia pigmenti and concluded that it was a familial disorder This case is not familial

DR WALTER F LEVER In several of the reported cases other abnormalities, such as ectodermal defects, were present in the patient as well as in members of the patient's family There is, however, only one report, that of Naegeli (cited by Sulzberger, M B, ARCH DERMAT & SYPH **38** 57, 1938), concerning the familial occurrence of incontinentia pigmenti Thus, the absence of a familial history is not against incontinentia pigmenti

DR WALTER F LEVER, Boston That would not explain the lesions on the forehead and scalp I agree with the presenter's diagnosis of dermatitis herpetiformis and would suggest that sulfapyridine be given in larger amounts I have observed a case in which there was no response until 6 Gm a day were given The patient has been taking that dose for six months, and it controls the eruption

DR JOSEPH GOODMAN, Boston What blood level of sulfapyridine was reached with that amount?

DR WALTER F LEVER, Boston I have done no determinations of the blood level

DR WILLIAM P BOARDMAN, Boston The patient told me that she was just as uncomfortable while taking sulfapyridine If the sulfonamide drugs are not well tolerated or are ineffective, why not try potassium arsenite solution (Fowler's solution) which has long been known to be effective in dermatitis herpetiformis?

DR JOSEPH GOODMAN, Boston The use of sulfapyridine in dermatitis herpetiformis interested me in relation to a patient I treated recently, starting as Dr Lever did and increasing to a maximum dose of 6 Gm a day My patient had typical dermatitis herpetiformis The drug was given in gradually increasing amounts over a period of three months At the end of that time she took 6 Gm daily for two and one-half weeks The blood level was slightly over 7 mg per hundred cubic centimeters, an adequate level of sulfapyridine The dermatitis did not improve more than 20 per cent It was a question whether 8 Gm a day would be effective The blood level seemed adequate, and I was a little uneasy about the situation as it was I wonder how many failures with sulfapyridine have been seen by the members of this society, with doses of 3 to 5 Gm daily as a maximum

DR OSCAR GILJE, Oslo, Norway (by invitation) I would like to hear about the treatment of dermatitis herpetiformis with diphenhydramine hydrochloride (benadryl®) Two patients in Norway whom I treated with benadryl® were relieved In 1 of the cases the disease was of six years' duration and in the other one-half year When benadryl® therapy was stopped, the itching became worse, the patients improved on resuming treatment with benadryl®

DR BERNARD APPEL, Lynn, Mass I questioned this patient about her reaction to benadryl® and she told me that it did not help her pruritus It did procure a good night's sleep and made her feel more relaxed but apparently did not relieve the itching I would agree with the diagnosis of dermatitis venenata due to rubber in the clothing The entire picture is consistent with that diagnosis, not only because of the definite, clear, smooth, symmetric pattern which corresponds to the articles of clothing worn that contain rubber but also because the rest of the eruption is consistent with it Contact dermatitis due to rubber from articles of clothing may produce generalized eruptions The presence of vesicles certainly does not contradict the diagnosis of contact dermatitis

DR JACOB H SWARTZ, Boston How often do you see clusters of scars in dermatitis from rubber?

DR BERNARD APPEL, Lynn, Mass Consequent reactions like crusting, follicular involvement, pigmentation and all the so-called "id" type of lesions depend, first, on the duration and, second, on the particular patient's sensitivity and intensity of reaction

Examination reveals an eruption limited to the dorsa of the hands and distributed over the region of the metacarpophalangeal joints The lesions consist of numerous solitary and grouped, milky white, hard nodules of uniform size, they are all 1 to 2 mm in diameter A few exhibit a faint narrow rim of surrounding erythema There is no tenderness now

A specimen was removed for histologic examination, and the diagnosis of "multiple epidermal cysts" was made Results of examinations of the chemical content of the blood, including calcium, cholesterol esters and fatty acids, were normal

DISCUSSION

DR MAURICE M TOLMAN The biopsy specimens were studied in several laboratories, all with the same diagnosis epidermal inclusion cysts, with some changes in the elastic tissue There was no evidence of xanthomatous infiltrate, or of colloid, as far as we know In the literature are reports of 3 such cases Ormsby presented one (Ormsby, O S Bullous Dermatitis [Pemphigus?], ARCH DERMAT & SYPH 28 246 [Aug] 1933) associated with pemphigus The lesions were in an area of the skin where pemphigoid lesions had healed, leaving these cysts In another instance, cysts came where there was vesiculation following exposure to the sun (Dietel, F *Dermat Wchnschr* 99 1637, 1934) The third patient had lesions at the sites of vesicles probably from dermatitis venenata We have all seen this occur in epidermolysis bullosa Apparently what takes place is a peculiar reaction to trauma The vesicular lesions heal entirely, and it is in the healing areas that one finds the origin of these epidermal cysts, representing some peculiar response of the tissue The patient is now improving, and we cannot find any reason for it, although she is now pregnant It might be that with the hormonal reaction there may be a nonspecific response She is about 50 per cent better

DR FRANCIS P MCCARTHY The histologic slides showed typical epidermal cysts which are seen so often in the lesions of epidermolysis bullosa One can explain the development of epidermal cysts in the latter disease but not so easily in a vesicular dermatosis on the basis of trauma

Tuberculosis Miliaris Disseminata Faciei Presented by DR FRANCISCO RONCHESE, Providence, R I

Berlock Dermatitis in the Form of a Band Across the Forehead Presented by DR G MARSHALL CRAWFORD, Boston

DISCUSSION

DR MAURICE J STRAUSS, New Haven, Conn I do not recall from the history that a perfume had been used, but, even if it had been, this should not be labeled Berlock dermatitis I would call it pigmentation following dermatitis The term Berlock dermatitis was coined to describe the disease in cases where perfume had been poured on and allowed to run down The word Berlock means pendant It is that particular configuration in which there is evidence of an irritating substance running down in streaks which should be kept as the original concept of Berlock dermatitis

DR WILLIAM B SWARTS, Greenwich, Conn The patient said that he had been employed as a bartender and that the eruption started in September I asked whether he served many Tom Collins drinks during the summer, because the use of lime oil is important The mechanism is the same as Berlock dermatitis except that the essential oil is sprayed over his face A patient of mine with dermatitis venenata of the face made the diagnosis herself and stated that she never got the

Multiple Epidermal Cysts of the Skin Presented by DR F RONCHESE, Providence, R I

A 14 year old white school girl, G deB , American-born of Portuguese parents, is presented with lesions which have been present on her face since birth They have not been observed to change appreciably with the passage of time She had



Fig 1—Multiple epidermal cysts of the skin The face of a 14 year old girl studded with milia, a few isolated lesions of keratosis pilaris and erythema

no hair anywhere until the age of 3 years, at that time a little began to appear on her scalp, and it developed slowly thereafter There were no eyebrows until the past few years, and no hair has developed elsewhere The patient has always been in good health There is no history of similar disturbances among other members of the family Negro ancestry was denied The patient seemed of normal intellect and was progressing well at school

3 0 cm One on the dorsum of the tongue was white on top, suggesting a secondary leukoplakic reaction The rest of the oral cavity was free of lesions

DR B J KENNEDY, Boston (by invitation) The woman was given urethane because of reports describing its use in leukemia and a few isolated carcinomas Urethane is called ethyl carbamate and is an ancient anesthetic for animals Haddon and Sexton (Influence of Urethane on Experimental Tumors, *Nature,* London **500** 157, 1946) found that phenyl carbamate and phenylurethane produced regression of mammary carcinoma in mice and Walker carcinoma in rats This led to investigation with urethane which produced the greatest effect, especially in the carcinomas There were scarring and decrease in the mitoses in the cells Another group from the same hospital began using urethane in human beings (Paterson, E , Haddow, A , Ap Thomas, I , and Watkinson, J M *Lancet* **1** 677, 1946) They tried it in 19 patients with myeloid leukemia, 13 with lymphatic leukemia and 13 with various types of carcinoma Among the last group only 4 (including patients with Hodgkin's disease and a salivary gland carcinoma) showed some regression of the tumor while the others had but little response The reaction in the patients with myeloid leukemia was striking In nineteen to forty-seven days the urethane produced a reduction in the white cell count of 20,000 or more cells It was found that this reduction of the white cells was chiefly in the neutrophils The hemoglobin did not seem to be affected, or the red cell count, and when the patients were given 100 Gm or more of the drug the hemoglobin rose an average of 27 per cent The patients with lymphatic leukemia showed a similar response but not as striking as did those with myeloid leukemia It was concluded that the urethane treatment of leukemia may be comparable to roentgen therapy The rise in hemoglobin, decrease in white cell count and reappearance of normal differential counts all followed the same pattern as would be expected with roentgen treatment Because of this and the close relation of mycosis fungoides to lymphomatous disease, urethane was given to this patient My co-workers and I plan to give it to a large series of patients to determine whether or not it is a drug that should be used in these cases This patient has been treated for almost two weeks, and the only response so far is perhaps some drying of the skin

DR JACOB H SWARTZ Have you read any reports citing granulocytopenia as a complication of this treatment?

DR B J KENNEDY, Boston (by invitation) Leukopenia develops in many of the patients If this reaction occurs, the drug must be withdrawn I have not heard of the occurrence of granulocytopenia

DR ARTHUR M SIMMONS What is the method of administration and dosage?

DR B J KENNEDY, Boston (by invitation) It is given orally, 1 Gm four times a day At present I do not believe that there is any definite dose that one can adhere to, we expect to try to increase the amount

Extensive Nevus Pilosus et Pigmentosus (von Recklinghausen's Disease?) Presented by DR G MARSHALL CRAWFORD, Boston

A Case for Diagnosis (Lupus Erythematosus? Tuberculosis Luposa?) Presented by DR ROBERT H GOLDFARB, Boston

Telangiectasia, Essential, Limited to Calves Presented by DR MAURICE M TOLMAN, Boston

C B , a 32 year old white housewife, is shown with changes on the backs of her legs which have been present for three and one-half years The patient first

follicular lesions on her forehead and similar changes on other areas where one finds Darier's disease I would suggest watching for the development of more evidence of keratosis follicularis

DR F RONCHESE, Providence, R I Dr Bernard Appel suggested to me the diagnosis of ulerythema ophriogenes This would be correct for the miliosis and the erythema, but there is no scarring The keratosis pilaris is limited to a few elements and the miliosis-erythematosis is not limited to the eyebrows but extends to the entire face However, this is an excellent suggestion, and an investigation will be made on the relation of this case to that rare entity which has been called ulerythema ophriogenes sive superciliare Tanzer, folliculitis rubra Wilson, keratosis pilaris rubra faciei Brocq and red keratosis pilaris Bazin This case is a good demonstration of the origin of milia in the hair follicle, the lesions eventually becoming keratosis pilaris, to be differentiated from the pseudomilia following epidermolysis bullosa or pemphigus and the miliary calcified sebaceous cysts It could be considered as a nevoid ectodermal defect

A Case for Diagnosis (Sinuses, Nodules and Ulcers of the Buttock Tuberculosis Colliquativa? Actinomycosis?) Presented by DR JACOB H SWARTZ, Boston

DISCUSSION

DR JACOB H SWARTZ, Boston I have two more tentative diagnoses to add symbiotic infection with Staphylococccus and Streptococcus, and dermatitis factitia plus infection I saw this man only once, and no laboratory work was done I will be glad to report on the case at the next meeting

DR FRANCIS M THURMON, Boston I suggest the diagnosis of dermatitis factitia It is asymmetric, and there was one lesion slightly stained, as though something had been applied, there were tiny white vesicles on the top

DR JOHN G DOWNING, Boston For three years I have been treating a man with a similar eruption, which started on his legs after contact with oil I have seen these eruptions on the arms following the same event Cultures from one patient showed that he had a synergistic combination of hemolytic Streptococcus and Staphylococcus

NOTE—A second biopsy specimen was subsequently removed from the patient's thigh, and a sinus tract found in the depth of the wound was curetted to obtain additional material for mycologic study Histologic observations were non-specific An extemporaneous preparation from curetted material revealed the "sulfur granules" of actinomycosis, and microscopic study showed the characteristic club-shaped formations Cultural studies were confirmatory

Scurvy Presented by DR GEORGE E MORRIS, Boston

E D, a 45 year old white man, formerly occupied as a welder, complained of an eruption *on the feet, legs and thighs of six weeks' duration The first lesion* appeared on the left thigh as a red scaly patch Three weeks ago the lower extremities rapidly erupted with dark spots all over the legs The patient has consumed considerable quantities of alcohol, and his diet was distinctly inadequate

At this time numerous fading purpuric blotches may be seen on the lower portions of the patient's legs and the dorsa of his feet The remainder of the lower extremities, the buttocks and lower portion of the trunk show a sparse eruption of small, brownish, scaly patches from 0 5 to 1 5 cm in diameter

York State J Med 46 2147 [Oct 1] 1946) who used with success in dyskeratotic dermatoses triolein ozonide, which is formed in olive oil on ozonization

DR NEVILLE KIRSCH, Hartford, Conn (by invitation) Sharlit has used ozonides in oil By rubbing in the oil four times daily his patients succeeded in eliminating keratotic lesions It has also been employed by MacKee The product may be obtained from G F Harvey & Company of Saratoga Springs, N Y, and must be refrigerated Twenty per cent of the ozonide mixture is incorporated in an appropriate base and rubbed in four times a day for six to eight weeks

DR WALTER F LEVER, Boston I have had no experience with ozonides, but I suggest treatment with 2,3-dimercaptopropanol (BAL) Since in this patient the arsenic preparation was given only two years ago, there may still be some arsenic remaining in her tissues, and it might continue to form keratoses BAL is effective in liberating organic arsenic from tissue

Dermatitis Herpetiformis (Contact Dermatitis from Rubber?) Presented by DR CARL A DAHLEN, Boston

T B, a 23 year old white girl, displayed an eruption of two years' duration, affecting the forearms, scalp, trunk and buttocks The first lesions appeared on the forearms in the form of vesicles At some later date the scalp became affected Lesions developed on the back and buttocks about a year ago Itching and burning have been severe, the patient claimed to be exhausted at times from these symptoms

On examination this young woman revealed a symmetric eruption affecting the scalp, forehead, elbows, dorsal aspects of the forearms, shoulders, scapular areas, lower part of the trunk and buttocks On the back is a transverse band of clear skin at the level between the brassiere and girdle areas The primary lesions are grouped vesicles and papules with crusted excoriations and pigmented scars These changes are most pronounced on the elbows, shoulders and hips The lines demarcating the clear zone across the back are rather sharp Both the upper part of the back and the girdle area below reveal a mild diffuse erythema, and there is a minimal amount of fine branny scaling on these regions On the upper part of the back there are three moderately distinct rectangular patches, which stand out from the previously defined changes One is seated transversely across the middle part of the back, the other two are vertically parallel to each other on the midscapular regions These patches are approximately 5 by 15 cm in size and display a perceptible thickening with more scaling than the surrounding skin

Results of an examination of the urine and a hemogram were normal Treatment included use of diphenhydramine hydrochloride (benadryl®) 0 05 Gm three times daily for five weeks, followed by sulfapyridine, 0 5 Gm, twice daily for two weeks Two suberythema doses of ultraviolet rays were given prior to the sulfonamide drugs There had been temporary improvement from these measures

DISCUSSION

DR FRANCIS M THURMON, Boston I agree with the diagnosis of dermatitis herpetiformis If sulfapyridine were used in larger dosage, it would be more effective

DR GEORGE SCHWARTZ, Boston I disagree This is contact dermatitis due to rubber inserts in her brassiere and girdle I had the patient put on her girdle, and the lower portion of the eruption formed a complete outline of the garment The dermatitis is now becoming generalized

Leukoplakia of the Penis. Presented by DR JOHN G DOWNING, Boston

J F, a 65 year old white man of Irish birth, a retired elevated railway conductor, is presented with the complaint of soreness and cracking of the prepuce for about two months The patient had applied only petrolatum This afforded no relief, and the condition had become steadily worse

Examination reveals a distinct thinning of the skin of the prepuce and also of the glans penis There is a constricting sclerotic band about 2 cm proximal to the free edge of the prepuce, this has been partially relieved by biopsy, and at that point where the biopsy specimen was taken there is a small crust The remainder of this band is characterized by the appearance of whitish plaques and streaks with several erosions and fissures

The diagnosis from histologic study was reported as leukoplakia There has been no treatment

DISCUSSION

DR FRANCIS P MCCARTHY, Boston Leukoplakia resembles kraurosis in the aged in the sense that there are interstitial changes and leukoplakia and erosion

DR BERNARD APPEL, Lynn The diagnosis of kraurosis of the prepuce was considered The microscopic examination ruled that out, because it did not show typical changes of kraurosis or atrophy

DR FRANCIS P MCCARTHY, Boston The depth of the biopsy specimen may be misleading A deep section is essential and special connective tissue stains are required in order to rule out kraurosis In spite of the histologic changes, I feel that this is kraurosis of the prepuce

DR WALTER F LEVER, Boston I would oppose the diagnosis of kraurosis The histologic picture of kraurosis is characterized by atrophy of the epidermis and degeneration of the collagen In this case there was neither The epidermis was acanthotic, and there was considerable hyperkeratosis The biopsy specimen extended a fair depth into the connective tissue, and it showed no evidence of degeneration There were numerous dilated capillaries and a chronic inflammatory infiltrate There was no evidence of carcinoma The histologic picture is consistent with senile keratosis or leukoplakia

DR FRANCIS P MCCARTHY, Boston In kraurosis there may be areas of atrophy and also leukoplakia with both hyperkeratosis and acanthosis

DR JACOB H SWARTZ, Boston I agree

DR JOHN G DOWNING, Boston There was no evidence of kraurosis or atrophy The skin was infiltrated, fissured and leukoplakic in appearance It probably would go on to cancerous degeneration if neglected This patient can be cured by excising the area affected

Leukoplakia of the Tongue, Buccal Mucosa and Lips, Syphilis Presented by DR F RONCHESE, Providence, R I

A D, a 38 year old white man of American birth, a truck driver, for the past three years had noted white patches on his tongue and lips and on the inside of his mouth The anterior portion of the tongue was raw for much of this time and was somewhat tender, but there was otherwise little discomfort Shortly after the appearance of these lesions the patient was found to have repeatedly positive serologic reactions to tests for syphilis No history referable to the date of infection was obtainable, previous genital or cutaneous lesions were denied No other relevant data were obtained The patient smoked from eight to ten cigars daily

DR JOSEPH GOODMAN, Boston I think that we are going far afield when we call this a contact dermatitis Let us assume, with Dr Schwartz, that this eruption corresponds exactly to the rubberized areas of the girdle It has spread to the forehead, scalp and elbows In contact dermatitis severe enough to produce a widespread eruption one must also expect a local extension I cannot conceive of a dermatitis of this sort spreading so widely without becoming generalized on the trunk I am sure that if these lesions were not in the area touched by her girdle, there would be no doubt about dermatitis herpetiformis

DR JOHN G DOWNING, Boston Two months ago this girl presented a classic picture of dermatitis herpetiformis, with the characteristic symptom of burning She showed grouping, pigmentation and atrophic scarring Today there is unquestionably a superimposed contact dermatitis which might be due to the elastic in the straps of her brassiere

DR CARL A DAHLEN, Boston There was considerable relief from treatment with benadryl,® but the patient failed to return The next time we saw her she had a recurrence I decided to give sulfapyridine, and it was prescribed in a dose of 0 5 Gm twice a day, but she still did not report back as instructed If she were cooperative, I might have obtained better results by increasing the sulfapyridine

DR FRANCIS P MCCARTHY, Boston This girl had a very interesting tongue She showed linear filiform papillae along the margins and beneath these areas were tufts of white hairlike papillae I made a diagnosis of depigmented congenital defect of the filiform papillae Some textbooks indicate that there are oral lesions in dermatitis herpetiformis I have never observed them, although I have been searching for years Has anyone here seen lesions in the mouth in dermatitis herpetiformis?

DR FRANCIS M THURMON, Boston I have seen 2 cases, one was shown to me in Chicago and the other was presented by me at a meeting of this Society

DR WALTER F LEVER, Boston I have seen 1 patient His eruption responded well to the usual doses of sulfapyridine, 2 to 3 Gm a day There was no doubt about the diagnosis

Lichen Planus of the Eyelids and Buccal Mucous Membranes Presented by DR WILLIAM J MACDONALD, Boston

Lichen Sclerosus et Atrophicus (Generalized) Presented by DR JOSEPH GOODMAN, Boston

DISCUSSION

DR JOSEPH GOODMAN, Boston This 43 year old woman has been followed in the clinic for six months At the start there was a hyperkeratotic follicular eruption characterized by small horny spicules She had alopecia when first seen, and this has extended since then It was thought at first that this was a vitamin A deficiency, but the vitamin A level and carotene level were normal In spite of that she received 200,000 units of vitamin A daily for a period of two months, during which time the eruption became worse The patient was then admitted to the hospital, and a biopsy was performed on the scalp lesions Those on the arms began to look like lichen planus and others have too, but at the same time many of the horny spicules seen when she was first observed in the clinic have persisted The picture presented today corresponds closely to the description of the disease called "lichen planopilaris" by Sachs and De Oreo (ARCH DERMAT & SYPH **45** 1081 [June] 1942)

DR FRANCIS P MCCARTHY, Boston That is a reasonable explanation, and the factitial element in this case may explain the unusual findings

Psoriasis, Keloids Following "Injections" Presented by DR LEO KORETSKY, Chelsea, Mass

A Case for Diagnosis (Erythema Multiforme Exudativum? Bullous Impetigo?) Presented by DR GEORGE SCHWARTZ, Malden, Mass

DISCUSSION

DR MILDRED L RYAN, Brockton, Mass I think that this 3 year old child has dermatitis medicamentosa She has had frequent attacks of asthma Has she been given any iodides or bromides?

DR GEORGE SCHWARTZ, Malden, Mass I saw this girl ten days ago At that time she presented bullae of ½ to ¾ inches (1 to 2 cm) in diameter, arising from normal skin They were on the arms, legs, abdomen and neck, there also were six or eight vesicles on the scalp I found nits and thought that she had bullous impetigo I have not seen her since then, and today she shows a different picture, one would think that she was another patient

DR S J MESSINA, Boston I think that this is a case of Loeffler's syndrome She had a high eosinophilic count and a history of asthma, which are characteristic of that disease There may or may not be an eruption which can suggest erythema multiforme I think that Loeffler's syndrome is a strong possibility in this case

DR JOHN G DOWNING, Boston I agree with the diagnosis of Loeffler's syndrome Recently I saw a patient with a history of asthmatic attacks, mottling on the chest and an eruption resembling erythema perstans on the chest, the blood picture showed a high eosinophil count

Dr Francis M Thurmon, *President*

Dr G Marshall Crawford, *Secretary*

New Haven, Conn, Oct 8, 1947

A Case for Diagnosis (Xanthomatosis?) Presented by DR MAURICE J STRAUSS, New Haven, Conn

E C, a 2 year old white girl, acquired a solitary lesion on the right cheek at about the age of 4 months This slowly increased in size, and gradually a few similar lesions developed around the original one The latter attained a size of 9 by 6 mm before excision six months ago They have been asymptomatic

On the right cheek there is a group of six small, solid, slightly elevated brownish red nodules each about 4 or 5 mm in diameter

Histologic examination revealed only a chronic inflammatory reaction

DISCUSSION

DR LEON BABALIAN, Portland, Me Although there is no regional enlargement of lymph nodes in this case, it is difficult to rule out lupus vulgaris

DR ALFRED HOLLANDER, Springfield, Mass My opinion is that these lesions belong to the group of localized xanthoma I did not study the slide too well, but the section did show some foam cells

There is a luxuriant growth of kinky hair on the scalp and the facial conformation is Negroid The face is reddish pink The skin thereon appears granular and feels slightly rough It is entirely covered with densely packed miliary lesions of 0 5 to 1 0 mm diameter, these are pearly white and smooth Diascopic examination shows complete blanching of the lesions No telangiectases can be observed The patient's eyebrows are sparse, scaly and also studded with milia The remainder of her skin exhibits no hair The lateral aspects of the arms and thighs reveal a sparse eruption consistent with keratosis pilaris, and a few isolated lesions on the face are similar in type No scars can be found anywhere

The Hinton reaction of the blood was negative Results of examination of the urine were normal A hemogram was normal with the exception of a leukocyte

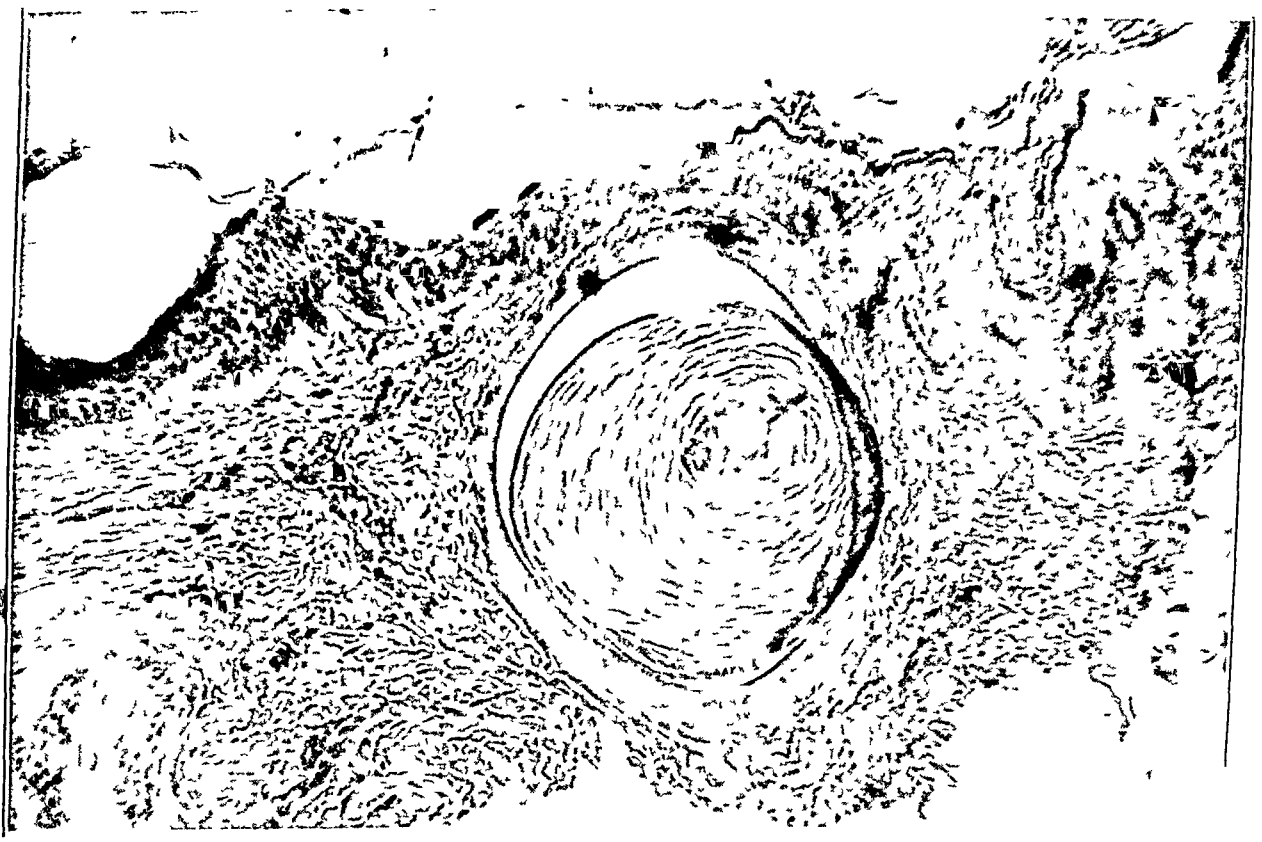


Fig 2—Multiple epidermal cysts of the skin Histologic section showing epithelial cysts

count of 10,750 cells per cubic millimeter The nonprotein nitrogen and glucose content of the blood were normal Histologic examination of a biopsy specimen revealed a moderate degree of hyperkeratosis There were cystic cavities about 0 2 mm in diameter just beneath the epithelium, these were lined with squamous epithelium and filled with a laminated keratotic mass No treatment had been administered until the past two months, during which time the patient has taken 200,000 units of vitamin A daily, there has been no appreciable improvement

DISCUSSION

DR JACOB H SWARTZ, Boston Although I am in accord with Dr Ronchese's diagnosis, I should like to point out that the patient had definite hyperkeratotic

treatment was discontinued Tripelennamine hydrochloride (pyribenzamine hydrochloride®), 50 mg four times a day, is of slight value at this time

DISCUSSION

Dr Bernard Appel, Lynn, Mass I think that the case is clinically typical of dermatitis herpetiformis and accept the diagnosis as presented The patient said urticarial reactions were so severe that he was completely covered with wheals Since sulfapyridine produces such a reaction, I suggest that tripelennamine hydrochloride be used in appropriate doses, I should prescribe 600 or 800 mg daily A patient with dermatitis herpetiformis who took sulfapyridine with fairly good results was recently given diphenhydramine hydrochloride (benadryl hydrochloride®) for a comparison She noted more lasting relief and recession of the lesions than with sulfapyridine One expects some trouble from sulfonamide drugs, and it is much safer to use tripelennamine or diphenhydramine in large doses

Dr Maurice M Tolman, Boston Since 1938 I have had under personal observation 3 patients with dermatitis herpetiformis who have taken sulfapyridine continually without reaction, and it controlled their disease I am a little afraid of continuing its use indefinitely We decided to try diphenhydramine and tripelennamine in doses of 600 mg daily in carefully controlled patients in the hospital but observed no relief from pruritus or diminution of the lesions We then administered sulfapyridine, there was immediate response, and remission took place

Dr Joseph Goodman, Boston On the other side of the picture, I should like to mention a patient who took sufficient sulfapyridine to produce a blood level of 7 mg per hundred cubic centimeters with but little effect on the dermatitis herpetiformis That patient has responded better to 400 mg of diphenhydramine daily than to the large doses of sulfapyridine One must thus conclude that some patients do better with one drug and some with the other I cannot maintain that sulfapyridine controls the disease in all patients with dermatitis herpetiformis, the same is true of tripelennamine and diphenhydramine

Dr Neville Kirsch, Hartford, Conn Some physicians in general practice have treated dermatitis herpetiformis with nicotinic acid

Hemangiolymphangioma of Tongue Presented by Dr Maurice J Strauss, New Haven, Conn

Sarcoidosis of Skin Presented by Dr E Myles Standish, Hartford, Conn

Adenoma Sebaceum Presented by Dr Maurice J Strauss and (by invitation) Dr Louis O'Brasky, New Haven, Conn

H M is a 12 year old white school girl About two months after she was born, her parents first noticed thickening under the toe nails and finger nails At the age of 7 years, papules appeared on the face Both parents are living and well and have no lesions of the skin although both are mentally defective One brother has a speech defect and is classified as mentally defective but shows no cutaneous abnormality Two brothers and two sisters are mentally and physically normal The patient herself is mentally normal

On the face there are numerous groups of small discrete white papules, symmetrically distributed over the forehead, on the sides of the nose and on the zygoma All the nails of the hands and feet are thin, soft and discolored, especially the nails of the great toes, and their growth is retarded There are brown fibrotic

The result of the tourniquet test was positive A hemogram was normal, including a count of the thrombocytes The patient has been given 2 quarts (about 2 liters) of orange and grapefruit juice daily for the past four days

DISCUSSION

DR WALTER F LEVER, Boston I suggest the diagnosis of Majocchi's disease In scurvy one has massive bleeding into the skin Here they are hemorrhagic punctate dots and erythema, as are commonly seen in Majocchi's disease

DR JOSEPH GOODMAN, Boston I agree that the lesions resembled Majocchi's disease, but in my opinion the patient has symptomatic purpura Whether or not he had scurvy could have been ascertained by a vitamin C determination, which was not on the record Since the treatment it would be impossible to say whether he had scurvy Follicular hemorrhages are characteristics of that disease

DR GEORGE E MORRIS, Boston When this man was seen last week he had the follicular hemorrhages which are typical of scurvy One may find large ecchymoses, but it is typically a punctate hemorrhagic disease Last week the result of a tourniquet test was strongly positive The patient was given a diet rich in vitamin C against my orders, and the result of the tourniquet test is now negative The eruption is disappearing That is not typical of Majocchi's disease

Dermatophytosis of the Extremities, Due to Trichophyton Purpureum

Presented by DR SEYMOUR J WHITE, Lawrence, Mass

An intradermal injection of 0 1 cc of Lederle's diagnostic trichophytin extract (1 30) gave rise to an immediate wheal reaction, within ten minutes it measured 1 5 cm in diameter, and numerous pseudopods soon appeared This reaction remained about twelve hours and left a persistent, erythematous, scaly patch, the result of a control injection of isotonic sodium chloride solution was negative Scales removed from the right palm and planted on Sabouraud's medium produced a growth identified as Trichophyton purpureum A biopsy specimen obtained from the left knee exhibited only nonspecific inflammation A number of fungicidal remedies have been applied for prolonged periods of time without response

DISCUSSION

DR JACOB H SWARTZ, Boston I suggest that the mycologic diagnosis be held in abeyance until the culture is more characteristic These lesions do simulate those seen with infection by the organism of Trichophyton rubrum (or T purpureum), but it might be Trichophyton gypseum

DR WALTER F LEVER, Boston Dr Swartz, do I understand that T rubrum or purpureum does not cause sensitization?

DR JACOB H SWARTZ, Boston That is correct, and I would not pay much attention to the immediate reaction A diagnosis should not be made on the cutaneous test alone, and I cannot do so on the strength of the culture as yet

DR FRANCIS P MCCARTHY, Boston Is this organism a possible contaminant or a true pathogen? I should like to know whether it is found on the skin normally

DR JACOB H SWARTZ, Boston I have never seen it as a contaminant

DR JOHN G DOWNING, Boston My co-workers and I cultured 100 specimens of normal skin of patients who had never had a fungous infection Specimens were taken from the scalp, the corners of the mouth, between the toes and the soles Pathogenic fungi were found in 2 cases, neither T purpureum nor Monila albicans (Candida) was isolated

Multiple Idiopathic Hemorrhagic Sarcoma of Skin Presented by DR M J MORRISSEY and DR H S REYNOLDS, Hartford, Conn

Aphthous Stomatitis Presented by DR MAURICE J STRAUSS, New Haven, Conn

Alopecia Cicatrisata Presented by DR MAURICE J STRAUSS, New Haven, Conn

Acarophobia Presented by DR ELLWOOD C WEISE, Bridgeport, Conn

Blastomycosis of the Skin Presented by DR MAURICE J STRAUSS and (by invitation) DR HARRY SIGEL, New Haven, Conn

H M, a 23 year old white electrician, first noticed a "pimple" on his left shoulder about a year ago For six months immediately preceding the development of this lesion he lived in Connecticut From September 1945 to February 1946 he was in Korea and from March to September 1945 in Okinawa Prior to that he lived in Idaho While in Okinawa, some "sores" developed on the back of his neck and on the extensor surfaces of both hands These healed spontaneously within about six weeks The lesion which marked the onset of the present condition grew slowly and progressively As the border extended, the central portion partly healed

There is now a large lesion on the left shoulder, about 18 cm long and 10 cm wide The border is circinate, bluish red, raised, rolled and indurated The marginal elevation slopes gradually toward the center of the lesion The border is most prominent at its medial edge, and there it appears somewhat verrucous Several portions of the margin are tender and exude small drops of pus on pressure The lateral edge of this lesion is flatter and more cicatricial

Direct microscopic examination of exudate from the lesion showed round, thick-walled, budding cells Cultural studies yielded a typical growth of Blastomyces dermatitidis hyphal with chlamydospores at room temperature and budding cells when incubated There has been no treatment administered

DISCUSSION

DR JACOB H SWARTZ, Boston I saw the slides and culture mounts and agree with the diagnosis of blastomycosis The culture was difficult to identify, as are all cultures in such cases The one grown at room temperature showed the hyphal type of growth with chlamydospores The one grown on Sabouraud's medium at incubator temperature exhibited the typical budding cells which are characteristic of Blastomyces Clinically the lesion was also compatible, with wartlike projections from the border The question at present is how to cure it I suggest a combination of sulfonamide drugs and roentgen rays Beyond that, I suggest ethyl iodide by inhalation Excision would be satisfactory if the condition is not systemic It is advisable to have a roengen examination of the chest and other structures that are liable to be involved, together with a complete neurologic examination and study of the spinal fluid The scar from a previous vaccination also shows early lesions of blastomycosis

DR ADRIAN SCOLTEN, Portland, Maine Must one go out of the country to acquire this disease?

The distal half of the dorsal aspect of this man's tongue is almost completely denuded of epithelium Within this area there are numerous small, white, infiltrated islands and some atrophic scarring The entire distal half of the tongue appears somewhat shrunken and atrophic, the margins are slightly elevated and are marked with alternate red and pearly gray striations The patient's lips and buccal mucosa also exhibit scattered small plaques of white atrophic tissue

Treatment has been carried on by the patient's family physician It consisted of fifty-five injections of bismuth salicylate and thirteen of oxophenarsine hydrochloride (mapharsen®) between May 1943 and October 1945 The dosage of these treatments was not known, there had been no clinical improvement The patient was smoking less during that time In March 1947 3,000,000 units of penicillin in oil and wax were administered, without detectable effect on the oral changes

The Hinton and Kahn reactions of the blood had both remained consistently positive up to the time of presentation Histologic examination of a biopsy specimen taken from the tongue revealed the following changes consistent with leukoplakia, acute ulceration and inflammation of the mucosa, with no evidence of malignancy

DISCUSSION

DR FRANCIS P MCCARTHY, Boston The erosion on this patient's tongue came on suddenly, and the ulceration has continued for three years As a result of inadequate treatment for syphilis there developed a smooth atrophy suggestive of glossitis luetica atrophica The failure of the ulceration to heal may be explained by interstitial connective tissue changes associated with limited blood supply from an old endarteritis I have recently studied syphilitic glossitis in postmortem specimens wherein interstitial sclerosis associated with decided narrowing of the lumen of arteries and atrophy of the overlying papillae are constantly found The granulation tissue as seen in this case does not become malignant, but the leukoplakic lesions in the periphery of the lesion may show a malignant tendency

DR JOHN G DOWNING, Boston When I first saw this man's tongue I was impressed by the sharp outline of the granulations and the intervening islands of leukoplakia I ordered two biopsies to eliminate malignancy, the diagnosis from both specimens was chronic inflammation I might suggest a diagnosis of stomatitis factitia I have seen 3 cases in which this condition was proved to be self-inflicted This man has syphilis, and I believe that he has been applying some strong chemical to his tongue to remove the previous leukoplakia

DR FRANCIS M THURMON, Boston Around the denuded areas there is definite leukoplakia of the tongue I think that the prognosis is serious, because once cancer of the tongue develops in a patient with tertiary syphilis there is no treatment that is successful

DR FRANCIS P MCCARTHY, Boston I am interested in what Dr Downing said because it seems unusual to see granulation continue so long without healing The blood supply is greatly diminished, and that may be a factor Why anyone should inflict a lesion of this kind on his own tongue is difficult to understand without some compelling motive such as the collection of compensation The patient told me that it developed overnight

DR F RONCHESE, Providence, R I If the changes on this man's tongue are regarded as potentially malignant, the entire surface should be removed with the coagulating loupe

DR JOHN G DOWNING, Boston Syphilis is in the background of this disease of the tongue, aggravated by a therapeutic attempt to cure it

Dr Francis M Thurmon, *President*

Dr G Marshall Crawford, *Secretary*

Dec 3, 1947

Necrobiosis Lipoidica Diabeticorum Presented by DR MAURICE M TOLMAN, Boston

Basal Cell Epithelioma, of Nose, Forehead, Left Eyebrow and Left Upper Eyelid Presented by DR JOHN G DOWNING and (by invitation) DR HARVEY B ANSELL, Boston

Tinea of Face (Microsporum Fulvum), Neurodermatitis Circumscripta of Wrist Presented by DR SEYMOUR J WHITE, Lawrence, Mass

Chronic Pemphigus of Eye with Cicatrizing Lesions of Skin Presented by DR BERNARD APPEL, Lynn, Mass

Frambesia Tropica (Yaws) Presented by DR JOHN G DOWNING, Boston

E R, an 8 year old Negro girl, has had lesions on the right heel and left gluteal fold for the past ten months The first lesion to develop was on the right sole, it appeared in December 1946 At that time the child resided in Jamaica, British West Indies, where a diagnosis of yaws was made Treatment consisted of one injection of a bismuth preparation and three of arsphenamine, and the lesion healed Another appeared on the right heel in July 1947, and the patient moved to Boston a month later She was first seen in the Boston City Hospital clinic in September 1947, and by that time another lesion had developed in the left gluteal fold There has been good response to therapy

Examination of the right heel when first seen three months ago revealed a raised, crusted, nontender granuloma, 1 5 by 1 5 cm This was surrounded by a 2 cm area of induration and scaling A similar, but smaller, lesion was present in the left gluteal fold but with less induration At this time there is little to be seen on either area The skin is slightly blacker than this moderately dark negroid integument, and a very indistinct trace of induration can be palpated

A dark field examination of material obtained from the lesions revealed organisms indistinguishable from Treponema pallidum The Hinton and Kahn reactions of the blood were positive on two occasions The hemoglobin content and red cell and white cell counts of the blood were normal, a differential smear revealed 48 per cent polymorphonuclear leukocytes, 42 per cent lymphocytes, 8 per cent monocytes and 2 per cent eosinophils Treatment consisted of intramuscular injections of penicillin, a total of 3,350,000 units was administered

Frambesia Tropica (Yaws) Presented by DR JOHN G DOWNING, Boston

D R, a 5 year old Negro boy, a brother of the preceding patient (E R), has lesions on the left heel and the buccal mucous membrane The first change appeared on this little boy's knee after an injury in April 1947 which failed to heal The ulcer was diagnosed as yaws and treated with three injections of a bismuth preparation plus seven of arsphenamine During the time of treatment several other lesions appeared on both legs, but all were healed by the time therapy was terminated He also came to Boston in August 1947 There was no further trouble

DR E MYLES STANDISH, Hartford, Conn I recall that about fifteen years ago I saw an almost exact counterpart of this lesion as far as color and induration are concerned, it proved to be lupus vulgaris

DR JOSEPH MULLER, Worcester, Mass I also thought of tuberculosis, but with pressure under a glass slide there was absolutely no sign of the typical apple jelly color that lupus vulgaris should show

DR ELLWOOD C WEISE, Bridgeport, Conn Although the light was poor where this little girl was shown, I thought that I could see a number of comedos in the affected area I have seen cases of precocious acne accompanied with chronic granulomatous lesions which were similar in appearance

DR BERNARD APPEL, Lynn, Mass I had the same first impression, but then I moved the baby into better light and saw that these pinpoint black dots were not comedos but little deposits of pigment My next feeling was that this was a nevus xanthomatosus I did not see the slide, but I do not consider the presence of foam cells essential

DR G MARSHALL CRAWFORD, Brookline, Mass There were definite small pigmentary deposits The possibility of a sebaceous nevus came to mind in view of the yellowish red color and firm consistency of the nodules I searched the section for foam cells but saw only a number of large pale reticulated structures which suggested portions of sebaceous glands cut at the edges

DR JACOB H SWARTZ, Boston This lesion may be given several different names It does not matter whether it is called nevus comedonicus or a sebaceous nevus, it falls into the same group I do not believe that a foam cell will ever be found

Granuloma Annulare Presented by DR MAURICE J STRAUSS, New Haven, Conn

Keratosis Follicularis Presented by DR ALBERT LEVENSON, Bridgeport, Conn

Dermatitis Herpetiformis Presented by DR CHARLES N SULLIVAN, New Britain, Conn

E S, a 42 year old white printer, first had severely pruritic lesions on the back of the left thigh four years ago, the eruption slowly spread and became generalized There have been several remissions and exacerbations, but the eruption has never completely cleared

There are groups of crusted papules, each lesion about 2 to 3 mm in diameter, scattered profusely over the trunk and extremities On the cheeks there are vesicles, some recently abraded and crusted There are many macular scars with pigmentation

Examination of the blood revealed nothing abnormal except 11 per cent eosinophils Microscopic examination of a biopsy specimen, reported by Dr Wilbert Sachs, of New York, showed the vessels of the middle and upper parts of the cutis dilated and the walls slightly thickened There was a perivascular infiltrate of small round cells and wandering connective tissue cells There was moderate interstitial edema in the upper part of the cutis The epidermis was regularly acanthotic, with an impetiginized cavity which had partially broken through at one point

Sulfapyridine relieved the pruritus but produced urticaria Sulfadiazine and roentgen ray treatment produced a remission, but the eruption recurred when this

finally sent back to the United States for that reason The lower lip
nvolved while he was in the South Pacific, but the condition has never
evere as on the upper lip

e present time the external appearance of the lips is grossly normal except
edema of the upper lip The inner aspect of the latter reveals intense
involving the two center fourths of the lip There is a depression
e affected area as though it had been drawn inward by scarring, but no
can be definitely made out A mild degree of maceration is present, and
ted area appears abraded The lower lip is similarly but much more
fected and only along the occlusal surface

s a private patient who was seen in consultation, and there was no oppor-
mitted for laboratory study None has been carried out elsewhere Treat-
the past has consisted of liver injections, arsenic drops, several unknown
, great quantities of vitamins and roentgen ray therapy More recently
of a gold preparation have been given (quantity unknown), these were
because of local reactions at the affected site In the last few months,
nt has received oxophenarsine hydrochloride (mapharsen®), and he feels
has been responsible for slight improvement

DISCUSSION

ERNARD APPEL, Lynn, Mass I have only an unhappy prediction to make
xperience in several similar cases the prognosis is bad The disease
and nothing I know of has done any of the patients any good

OHN G DOWNING, Boston On close examination, the glandular orifices
ly visible, owing to dilatation of the ducts There is a sticky secretion
nosis is cheilitis glandularis apostematosa

WILLIAM R HILL, Boston In the last two years I have observed 4
with dermatitis of the lips somewhat similar to that which this patient
Three patients related the onset of their eruption to exposure to sun
e sailors in the Caribbean area, and their disease was diagnosed as lupus
tosus, they were treated with bismuth and gold preparations without
During the period of observation 1 of these men had a typical eruption
c eczema on the back of the hands, and the thought occurred to me that
the disease was a virus infection With this in mind, I treated 2 patients
llpox vaccine but noted no improvement

G MARSHALL CRAWFORD, Brookline, Mass This man is not my patient
m five or six years ago when his complaint first began and there was
present except a small fissure which had healed during the winter months
recurred He went to war but was discharged from the service because
lips, receiving treatment from several sources as indicated in the history
y saw him again in consultation I was not satisfied with the diagnosis
ited, and yet I could not deny it Nevertheless, I think that there is a
y that he may not have lupus erythematosus Without other lesions, the
s an enigma

WILLIAM R HILL, Boston Does the fact that the lips respond to
or gold help in the diagnosis of lupus erythematosus?

MAURICE M TOLMAN, Boston I have searched steadily for a case of
ythematosus discoides limited to the mucous membrane I have heard of
es but have yet to see one I am inclined to think this is not lupus ery the-

tumors under most of the nails, elevating the plate from the bed The extensor surfaces of the arms and legs, the back and the buttocks are dry with follicular hyperkeratosis

Examinations of the blood and urine showed normal conditions The Kahn reaction of the blood was negative

DISCUSSION

DR ALBERT LEVENSON, Bridgeport, Conn I should call this a case of milium Clinically the lesions do not resemble those of Pringle's adenoma sebaceum

DR ALFRED HOLLANDER, Springfield, Mass I definitely exclude Pringle's disease I feel especially that the numerous lesions on the forehead are those so often seen in the common type of acne and that if one tried to remove them, one would find some to be comedos, some to be milium-like and some to be hygromas Further inspection of the face revealed other small comedo-like lesions The lesions on the face fall partly into the acne group and partly into the hygroma group Those on the forearms should be classified as keratosis pilaris

DR G MARSHALL CRAWFORD, Brookline, Mass I agree with what has been said, but I insist on the diagnosis of tuberous sclerosis, also making a plea that all such cases be called tuberous sclerosis Adenoma sebaceum and other subsidiary diagnoses may be added as presented by each individual patient The cutaneous and visceral anomalies reported in cases of tuberous sclerosis are almost beyond enumeration A wide variety of cutaneous changes occur Most characteristic are the subungual keratoses which in this girl involve every one of her twenty nail beds She does not show the characteristic adenoma sebaceum, as every one else has said The milium-like changes do not exclude the diagnosis of tuberous sclerosis, neither do the keratosis-pilaris-like changes, which in this case are not limited to the usual areas but are diffuse The entire skin shows varying degrees of follicular hyperkeratosis There is also a background of mental deficiency and other abnormalities, which is entirely characteristic of tuberous sclerosis

DR EARL GLICKLICH, Boston I have observed a case of adenoma sebaceum in which it was necessary to have fundus examinations for additional information to make a diagnosis Such an examination usually shows a strawberry or mulberry type of growth on the fundi I suggest that an ophthalmologist examine this patient's eyegrounds

DR G MARSHALL CRAWFORD, Brookline, Mass There should also be roentgen examinations of the chest and kidneys, since polycystic kidneys and various other visceral changes are much commoner than is usually supposed

Erythroplasia of Queyrat, Penile Presented by DR MAURICE J STRAUSS, New Haven, Conn

Dermatitis Exfoliativa Presented by DR MICHAEL J MORRISSEY and DR HARRY S REYNOLDS, Hartford, Conn

Squamous Cell Carcinoma of Leg, Blastomycosis? Presented by DR ELLWOOD C WEISE, Bridgeport, Conn

Multiple Idiopathic Hemorrhagic Sarcoma of Skin Presented by DR MAURICE J STRAUSS, New Haven, Conn

Chronic Pyoderma (Staphylococcus Aureus) Presented by DR GEORGE MORRIS, Boston

A Case for Diagnosis (Sarcoid? Tuberculid?) Presented by DR BERNARD APPEL, Lynn, Mass

Hodgkin's Disease of the Skin Presented (by invitation) by DR PAUL J CATINELLA, Boston

D F, a 34 year old white housewife of Irish birth, presents a lesion on the front of the left thigh which is said to be of only nine weeks' duration It appeared first to be a small blister and then became a shallow ulcer which gradually enlarged The lesion had been asymptomatic

At the time of first examination, several weeks ago, a solitary lesion was found on the anteromedial aspect of the patient's left thigh about 4 inches distal to the inguinal ligament This proved to be a moderately shallow circular ulcer of 2 5 cm diameter The center portion of the base of the ulcer was slightly raised, granulomatous and moist on the surface The borders were firm, and the tissue about the periphery was deeply infiltrated

A biopsy specimen was obtained, and the histopathologic examination revealed changes indicating a diagnosis of Hodgkin's sarcoma The white cell count of the blood was 2,750 per cubic millimeter, a differential smear revealed 56 per cent polymorphonuclear leukocytes, 38 per cent lymphocytes, 3 per cent monocytes and 3 per cent eosinophils Roentgenologic examination of the chest, lumbosacral portion of the spine, pelvis and hips revealed nothing abnormal except a "condensing osteitis of the right ilium"

The patient's lesion was widely excised two weeks ago The scar is soft, without suggestion of recurrence

DISCUSSION

DR FRANCIS M THURMON, Boston What is the prognosis in this case?

DR JOHN G DOWNING, Boston We should raise the question of further therapy at this point Have sufficient measures been taken?

DR BERNARD APPEL, Lynn, Mass When I first saw the patient, I considered this to be syphilis, probably an unusual extragenital chancre A week or so later this was an oozing, exuberant, red, moist, granulating, mushroom type of lesion with the edges firm and curled outward, and then it looked like either a rapidly growing carcinoma or sporotrichosis, or perhaps one of the other mycotic granulomas The last thing in my mind was Hodgkin's disease, and when I heard the microscopic diagnosis I could hardly believe it, yet the slide shows cells of the immature lymphoblastoma type that are consistent with Hodgkin's disease

DR MAURICE J STRAUSS, New Haven, Conn As the patient was presented today, there was no lesion to be seen However, having now looked at the colored photograph, I feel that we would be justified in making a diagnosis of mycosis fungoides of the tumor d'emblee type It is not always easy to tell mycosis fungoides from Hodgkin's disease microscopically, and it is quite possible that this error could occur I recall a similar case presented to this Society several years ago at a meeting at New Haven, Conn The man died six years later, I believe in an accident, and had never had any known recurrences The lesion was in the lumbar region, and a simple but wide excision was performed with skin grafting

DR JACOB H SWARTZ, Boston No It is named North American blastomycosis only to differentiate it from European blastomycosis

DR MAURICE J STRAUSS, New Haven, Conn *Is there any particular sulfonamide preparation which should be chosen?*

DR JACOB H SWARTZ, Boston I have had little experience in the use of sulfonamide drugs in treatment of blastomycosis, but several drugs of that group have been successfully used Iodides should not be used until after an intradermal test with blastomycin has been made It may be necessary to desensitize the patient before administering iodine compounds The same applies to patients with moniliasis

DR ALBERT LEVENSON, Bridgeport, Conn I should like to ask Dr Swartz whether the danger in giving sodium iodide is due to the fact that the patient has blastomycosis Sodium iodide is used in many conditions

DR JACOB H SWARTZ, Boston I believe that the form of iodide does not matter It is the allergic factor that counts The principle is the same as that in giving iodides to a patient with tuberculosis The reaction is on an allergic basis and may be compared to a Herxheimer reaction Any patient with a systemic fungus infection may be a poor risk

DR HARRY SIGEL, New Haven, Conn (by invitation) I saw several patients with blastomycosis of the skin in a military hospital, and all of them were treated with iodide without previous desensitization Though they were not previously *tested for allergy to blastomycosis, none of those patients had ill effects*

Pemphigus Erythematosus Presented by DR MAURICE J STRAUSS, New Haven, Conn

Foreign Body Granuloma in Skin of Finger Presented by DR E MYLES STANDISH, Hartford, Conn

Hidradenitis Suppurativa Presented by DR MAURICE J STRAUSS and (by invitation) DR CARTER MARSHALL, New Haven, Conn

Erythema Multiforme Presented by DR WILLIAM B SWARTS, Greenwich, Conn

Hemangioma of Left Thigh and Leg Presented by DR MAURICE J STRAUSS and (by invitation) DR HARRY SIGEL, New Haven, Conn

A Case for Diagnosis (Leishmaniasis of Skin?) Presented by DR ALBERT LEVENSON, Bridgeport, Conn

Tuberculosis Luposa Presented by DR MAURICE J STRAUSS, New Haven, Conn

Tuberculosis Luposa, Cutaneous Horn Presented by DR MAURICE J STRAUSS, New Haven, Conn

Bowen's Disease Presented by DR WILLIAM B SWARTS, Greenwich, Conn

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

Herman Sharlit, M D, *Chairman*

Maurice J Costello, M D, *Secretary*

Jan 7, 1947

Erythema Induratum Without Ulceration Presented by Dr Maurice J Costello

P M, a Puerto Rican woman aged 27, is presented from the Dermatologic Clinic of Bellevue Hospital with an eruption involving the thighs and the lower third of each leg of about one year's duration The patient had pulmonary tuberculosis ten years ago, but she states that a recent roentgenogram of her chest showed arrested pulmonary disease, and examinations of the sputum did not reveal tubercle bacilli Her menses are normal A brother and sister died of tuberculosis

The patient states that her eruption began as small red papules which were painful and frequently broke down and drained pus (This was not verified in the four months the patient has been under observation in this clinic) The lesions become painful when she arises each morning and also on exposure to cold

The eruption is present on the lower thirds of the legs and about the ankles and consists of scattered, erythematous, scaly, nodular and plaque-like lesions, some of which are fluctuant but do not drain pus Others are indurated

A section of the skin showed mild acanthosis of the epithelium, with some downgrowth of the rete pegs into the corium In the superficial and deep corium numerous granulomatous lesions were seen These consisted of indistinct epithelioid cells with occasional multinucleated giant cells in the central portions There was some proliferation of fibrous tissues and young blood vessels about these nodules A moderate infiltration of lymphocytes and large mononuclear cells and a few polymorphonuclear and plasma cells were present throughout the corium but primarily in the granulomatous lesions In and about the lesions there were varying numbers of mononuclear cells filled with brown granular pigment Deep in the corium some normal adipose and glandular tissue was seen Elastic tissue staining revealed the absence of elastic fibers through the upper corium wherein the tubercles were seen The histologic diagnosis was erythema induratum

The patient underwent thoracoplasty about ten years previously A roentgenogram of the chest three days ago showed no activity

DISCUSSION

Dr S Irgang It is not possible to make a definite diagnosis of erythema induratum in this case because the subcutis was not included in the section That is the layer in which the typical changes of this disease are found

Dr Fred Wise The diagnosis of erythema induratum is made in this case by clinical observation alone I should say that this is the typical textbook picture of erythema induratum of the Bazin type The characteristic histologic changes occur in the deeper veins especially, but a clinical diagnosis is acceptable in this instance A histologic diagnosis can be made, even in the absence of tubercle formation

until October 1947, when a lesion appeared on the left heel which was subsequently diagnosed in the Boston City Hospital as yaws Another lesion was discovered on the left buccal mucous membrane at that time

When examined in October, this little boy revealed a superficial ulcer on the left heel It was 1 5 by 1 5 cm, with slightly elevated margins and was not tender Treatment was not started for about a week, and during that time the entire lesion became raised, with the appearance of a chronic granuloma, and was distinctly indurated The lesion on the left buccal mucous membrane consisted of a shallow ulceration measuring 6 by 6 mm , no induration could be detected There were numerous enlarged, nontender posterior cervical and inguinal lymph nodes At present there is nothing on the left heel except a trace of deeper pigmentation The buccal mucous membrane exhibits no change of any kind

Dark field examination revealed organisms indistinguishable from Treponema pallidum The Hinton and Kahn reactions of the blood were repeatedly positive The white cell count of the blood was 13,400, and the red cells numbered 3,640,000 per cubic mm , a differential smear contained 48 per cent polymorphonuclear leukocytes, 50 per cent lymphocytes and 2 per cent monocytes Treatment consisted in administration of 4,000,000 units of penicillin by intramuscular injection

DISCUSSION OF CASES OF FRAMBESIA TROPICA

DR JOHN G DOWNING, Boston At the June Meeting of the American Dermatological Association, Dr Rein reported a series of 1,000 cases of yaws, in all of which the clinical lesions disappeared under treatment, but the serologic reactions became negative in only 15 per cent He gave 1,200,000 Oxford units In the discussion of that report, others who had had experience with yaws stated that the reactions of as high as 40 per cent of their patients remained positive It was clearly indicated that large doses of penicillin are needed to cure this disease, greater quantities will result in better clinical and serologic response

Tuberculosis Luposa Presented by DR. JOSEPH GOODMAN, Boston

Idiopathic Macular Atrophy of Skin Presented by DR WILLIAM R HILL, Boston

Hemangiolymphangioma of Skin Presented by DR S J MESSINA, Boston

A Case for Diagnosis (Mycosis Fungoides or Late Cutaneous Syphilis?) Presented by DR WILLIAM R HILL, Boston

Lupus Erythematosus, Restricted to Lips Presented by DR G MARSHALL CRAWFORD, Brookline, Mass

W G, a 23 year old white American student, presents lesions on his lips of six years' duration This difficulty began as a single fissure in the center of the upper lip which refused to heal It became worse every summer and was aggravated by any exposure to heat At first it would heal in the winter, but it has become worse with the passage of time and now does not heal at any time The fissure spread to become a raw area which slowly extended inward and upward It has been most uncomfortable throughout most of this time, and the greatest discomfort is on the inner aspect of the upper lip Smaller lateral lesions appeared later Two years ago the area measured 2 cm in length (transversely) and was

A Case for Diagnosis (Erythroderma Ichthysiforme?) Presented by DR FREDERICK REISS

E G, an unmarried Puerto Rican woman aged 39, was admitted to the dermatologic service of Bellevue Hospital in October 1945 because of a generalized exfoliating erythroderma, which, however, did not include the mucous membranes The past history and the family history were not contributory There was no history of allergy, of ingestion of drugs or of any previous antisyphilitic therapy According to the patient, the eruption started on the face and neck about eight months previously and gradually spread over the entire body At the onset, blisters were present She had always lived in Puerto Rico until the fall of 1945

The patient has remained hospitalized up to the present During this period the clinical picture has been essentially unchanged except for the progressive development of generalized erythroderma and keratoderma, particularly of the palms and soles, and pronounced alopecia of the scalp During the first year of hospitalization there was a weight loss of 40 to 50 pounds (18 to 22 7 Kg), but during the past six months the weight has remained constant at approximately 80 pounds (36 3 Kg) The appetite has been good during the entire course There have been occasional febrile episodes, with the temperature rising to 102 to 103 F for twenty-four to forty-eight hours at a time

At present the skin over the entire body is erythematous and scaly The palms and soles present a decided keratoderma The nails are dystrophic, thickened and extremely brittle In addition, there are slight generalized lymphadenopathy and almost total alopecia

Reaction of the blood to the serologic test for syphilis was negative Repeated urinalyses showed a normal reaction A complete blood count revealed a hemoglobin content of 9 5 Gm, erythrocytes 3,520,000 and leukocytes 8,700, with 53 per cent polymorphonuclear leukocytes, 41 per cent lymphocytes and 6 per cent eosinophils Routine chemical examinations of the blood all gave essentially normal findings The basal metabolic rate was +36 per cent The reaction to the congo red test for the presence of amyloid was negative

Biopsy showed a nonspecific picture of acanthosis and hyperkeratosis

Additional laboratory investigations gave the following results The blood sugar was 92 mg per hundred cubic centimeters and the nonprotein nitrogen 27 mg The albumin-globulin ratio was 3 2 to 2 6 Gm per hundred cubic centimeters The blood chloride level (expressed as sodium chloride) was 456 mg per hundred cubic centimeters The serum cholesterol level was within normal limits The blood calcium was 10 4 mg per hundred cubic centimeters, and the serum potassium level was 16 2 mg The twenty-four hour urinary output of ketosteroids was 7 mg (normal, 10 to 15 mg)

DISCUSSION

DR FRED WISE It is possible that Dr Reiss' diagnosis is the correct one, but I believe the diagnosis of pemphigus vegetans should be entertained

DR FRANK C COMBES I have observed this patient for the better part of a year, as have other members of our staff I can well understand how, on looking at her for only a short time, Dr Wise might consider pemphigus However, this patient has never had any bullae, and at no time have we entertained this diagnosis I have never observed a dermatosis of exactly this nature Her palms are remarkable Here there is some erythema, but the most prominent feature is the hyperkeratosis, which is not that usually observed on the palms and soles It actually accentuates the normal cutaneous markings No topical therapy has succeeded in

matosus This man has a protruding lower lip I have seen a number of men within the ages of 18 to 25 with carcinomatous degeneration of the lower lip following extensive exposure to sun I have also seen lupus erythematosus of the lip which soon developed into carcinoma, and I think this patient will have carcinoma Lupus erythematosus of the mucous membrane does not respond well to bismuth

DR BERNARD APPEL, Lynn, Mass Several years ago I saw a middle-aged woman with lesions on the inner aspect of the lower lip that looked like either lichen planus or the climacteric type of leukoplakia The eruption turned into a *more classic lichen planus and subsequently spread onto the buccal mucosa* A biopsy was done and the microscopic examination showed either lupus erythematosus or chronic inflammatory reaction of mucous membrane It was not until two or three years later that the lesions finally extended onto and beyond the vermilion borders of both lips, showing the classic cutaneous changes Although, strictly speaking, that disease was not limited to the mucous membrane, nevertheless it started there and was localized there for a long time Going back to the present case, I feel that this is more likely to be lupus erythematosus of the mucosa and less likely to be carcinoma of the lip

Pityriasis Rubra Pilaris Presented by DR LEON BABALIAN, Portland, Maine

Lichen Nitidus Presented by DR E A LAFRENIERE, Arlington, Mass

Lichen Planus Presented by DR GEORGE MORRIS, Boston

Case for Diagnosis (Nevus Linearis? Linear Lichen Planus?) Presented by DR GEORGE MORRIS, Boston

Multiple Idiopathic Hemorrhagic Sarcoma of Skin *Presented by DR G* MARSHALL CRAWFORD, Brookline, Mass

Pseudoxanthoma Elasticum of the Neck with Angioid Streaks Presented by DR JOHN ADAMS JR, Boston

This case provides a classic picture of pseudoxanthoma elasticum, first described by Balzer in 1884 *It may be located on the flexor folds, the axillas, the upper* and inner surfaces of the thighs and the abdomen, and in very rare cases the mucous membranes are also affected The lesions are asymptomatic but may persist for years Areas of calcification have been reported in the affected parts The angioid streaks of the retina, as noted in this patient, occur in about 25 per cent of the cases They are probably a part of a generally defective elastic tissue Hypertension may be found in some of the patients and also degeneration of the elastica of the larger arteries This might account for the hemorrhages which occur in various organs, including the brain The cause is unknown, and the disease is harmless

Leukemia Cutis (Type Unspecified) Presented (by invitation) by DR PAUL J CATINELLA, Boston

Lymphatic Leukemia with Herpes Zoster, Generalized Presented by DR S J MESSINA, Boston

A Case for Diagnosis (Erythema Bullosum? Pemphigus Vulgaris?) Presented by DR H VICTOR MENDELSOHN

A Case for Diagnosis (Macular Atrophy? Lymphogranuloma Venereum) Presented by DR FRANK C COMBES

Sarcoidosis Presented by DR H VICTOR MENDELSOHN

A Case for Diagnosis (Periarteritis Nodosa?). Presented by DR FRANK C COMBES

A D, a woman aged 35, was first admitted to the dermatologic wards at Bellevue Hospital in June 1946 presenting irregular, erythematous, urticarial lesions, widely scattered over the extremities and buttocks The lesions had first appeared approximately two weeks prior to this admission No previous history of asthma, hay fever, eczema, urticaria or other allergic manifestation was obtained Likewise, there was no family history of any allergic disorders

The eruption began with a few urticarial lesions on the thenar eminence of one hand, the wrist of the same hand and the buttocks The gradual appearance of similar lesions on the trunk and on other extremities was subsequently noted No pertinent past history was obtained The patient had undergone cholecystectomy in December 1944 for chronic cholecystitis and cholelithiasis She gave no history of having received any of the sulfonamide drugs

During July 1946, diffuse erythema, edema and doughy induration involving the left side of the face, the shoulder girdle, the upper part of the arms and the lower eyelids developed During the course of this episode, which lasted for almost one month, the patient became toxic and continued to run a temperature which ranged between 100 and 103 F Occasional vesiculobullous lesions appeared on the soles, the dorsa of the feet and the legs This acute picture disappeared gradually, and since the middle of August 1946 the patient has continued to show the present picture of a generalized, scattered urticarial eruption, with periods of exacerbation and partial remission

The urine has repeatedly shown traces of albumin and only occasional red blood cells Studies of renal function with phenolsulfonphthalein intravenously showed a 60 per cent excretion after two hours Repeated hemograms showed mild hypochromic anemia and constant eosinophilia, which has varied between 10 and 21 per cent

Examination of the stools showed no ova or parasites Intradermal tests for trichiniasis gave a delayed positive reaction after about twelve to nineteen hours Reactions to precipitin tests for trichiniasis were negative on two occasions Aspiration of sternal marrow revealed a normal picture Roentgenograms of the chest showed no infiltrations or other evidence of pathologic changes Roentgenograms of the skull and long bones revealed no abnormalities, and there was no evidence of calcification in the muscles Chemical examination of the blood showed no abnormalities with the exception of an increase in the serum cholesterol, which has ranged from 286 to 400 mg per hundred cubic centimeters

Biopsies of skin and muscle repeated on three occasions have failed to show any specific histologic picture The most recent biopsy of the skin, performed in November 1946, showed a diffuse vasculitis throughout the reticular layer of the corium and the subcutaneous tissue In addition, there appeared to be some proliferation of the intima and a granular degeneration of the walls of the involved vessels, with an accompanying pronounced perivascular infiltration which consisted for the most part of polymorphonuclear leukocytes and eosinophils

For all practical purposes, that is what has been done upon the patient presented today, and it may well be all the treatment that will be necessary

DR WALTER F LEVER, Boston The histologic section was densely infiltrated with anaplastic and immature reticulum cells Some of them had large nuclei, and others were multinucleated It is perhaps best to call this lesion a reticulum cell lymphoma Concerning the prognosis, I agree with Dr Strauss It is not uncommon for reticulum cell lymphoma to start as a single lesion on the skin or elsewhere, and if this lesion is excised completely there may be no recurrence

DR LEON BABALIAN, Portland, Maine Dr MacKee advised wide excision followed by irradiation

DR WALTER F LEVER, Boston I do not believe that irradiation is generally done Most lesions are in lymph nodes, where irradiation is impractical Radical excision is best, irradiation is optional

DR BERNARD APPEL, Lynn, Mass The matter of terminology of this group of tumors is still undecided When the proponents of the various terms get together and agree on what to call these cells, they may find that they are all talking about the same thing I think that if Dr Catinella were to go to the pathology department of the hospital with which I am associated and look up the original biopsy slides, he would find that they correspond closely to the section exhibited today Many of us have seen a solitary lymphoblastoma cured by surgical excision This will probably turn out to be that type of case

DR PAUL J CATINELLA, Boston (by invitation) I am sorry that the members did not have the benefit of all of the slides Sections of specimens taken a week later showed a picture resembling reticulum cell sarcoma except for one feature which established the diagnosis of Hodgkin's sarcoma That was the presence of multinucleated and polymorphonuclear giant cells of the Dorothy Reed type Wide excision was advised in the hope that if the lesion had started in the skin, eradication of the primary focus might be followed by a cure It was a long chance If the condition were not treated, the prognosis for life would vary from one to three years

DR JOHN G DOWNING, Boston The most complete monograph on lymphomas is that of Jackson and Parker (Jackson, H, Jr, and Parker, F, Jr Hodgkin's Disease and Allied Disorders, New York, Oxford University Press, 1947) It covers about every phase of this group of diseases, is clearcut and presents a clever classification according to life expectancy The reason I inquired about treatment is that we consulted Jackson, and he suggested excision, adding that the quicker excised, the more chance this patient had of living

Keratosis Follicularis Presented by DR FRANCIS M THURMON, Boston

Aneurysm of Transverse Aorta Presented by DR GEORGE MORRIS, Boston

Xanthoma Diabeticorum and Lipemic Retinitis Due to Diabetes Mellitus Presented by DR BERNARD APPEL, Lynn, Mass

Psoriasis in a West Indian Negro Presented by DR S J MESSINA, Boston

Sarcoidosis of the Skin Presented by DR WALTER F LEVER, Boston

Trichophyton Violaceum Infection of the Scalp Presented by DR FREDERICK REISS

S G, a white boy aged 8, is presented from the Dermatologic Clinic of Bellevue Hospital with lesions of the scalp of four months' duration

Shortly after the patient's arrival from Greece about four months ago, small areas of alopecia were noted on the scalp These fluoresced poorly under the Wood light, and some patches had few, but noticeable, "black dots"

Potassium hydroxide preparation showed spores situated inside the hair shaft A culture on Oct 10, 1946, was sterile Culture on November 13 yielded Trichophyton violaceum

DISCUSSION

DR EMANUEL MUSKATBLIT This condition is relatively rare in the United States Such cases may escape attention when, as in this instance, there are few foci, probably a quarter of an inch (0 64 cm) in diameter, which do not show the typical broken hairs In such instances the condition may not be revealed by examination under the Wood light This case will probably require epilation with roentgen rays, and even with that the infection may not be easy to eradicate

DR GEORGE M LEWIS In Russia, Trichophyton violaceum is one of the common pathogens One of our recent visitors to this country confirmed that fact and showed me pictures of some of the generalized eruptions as well as of typical involvement of the scalp and nails I can attest to the difficulty of curing the patients They are apt to pass from clinic to clinic, they receive roentgen ray epilation in a clinic that performs epilation well, and then several foci will be found to have been left, and it is difficult to say how they escaped treatment Dr Fox, if he were here, would probably comment on a patient who had had three epilations It was a considerable time after the last epilation before the hair returned The condition finally cleared One must be careful, in considering roentgen ray epilation in these patients, to ascertain whether epilation has been done previously

DR FREDERICK REISS The point which Dr Lewis brought out about the wide dissemination of such cases in Russia is interesting, but there is another remarkable point In Russia, T violaceum was frequently the cause of a deep-seated inflammatory reaction, while this fungus according to our experience causes only superficial involvement

Extensive Pigmentary Changes Following Bismuth Therapy Presented by DR MAURICE J COSTELLO

Herman Sharlit, M D, *Chairman*

Maurice J Costello, M D, *Secretary*

Feb 4, 1947

Darier's Disease in Mother and Daughter Presented by DR SAMUEL M PECK

Granuloma Inguinale with Extragenital Lesion on the Cheek Presented by DR MAURICE J COSTELLO

DISCUSSION

DR MAURICE J COSTELLO It was interesting to note that this patient was presented at another dermatologic society the other night without a complete history, and the consensus of those present was that she might have scrofuloderma This

DR S IRGANG In the absence of ulceration, it is not possible to differentiate erythema induratum clinically from nodular nonsuppurative panniculitis In view of the equal distribution of lesions about the legs and also because of the absence of a single ulcerated lesion during a period of fourteen months, I favor a clinical diagnosis of nodular nonsuppurative panniculitis

DR CHARLES WOLF To make a diagnosis of erythema induratum without real corroboration is rather risky I had the experience recently with a patient who had a solitary lesion on the calf of the leg for six months, with a history of pulmonary tuberculosis and thoracoplasty I took it for granted that the lesion was erythema induratum I was to perform a biopsy, but after one visit the lesion healed so much that I thought biopsy unnecessary The surgeon thought the patient should go back into the hospital for further operative treatment because of infection in the pleura I told him the cutaneous lesion was a manifestation of tuberculosis, and he removed it while operating on the chest Biopsy revealed chronic inflammatory tissue The patient presented tonight may have undergone a thoracoplasty, but the lesion on the leg may be an entirely different entity Therefore, we must have further evidence before we can accept it as Bazin's disease

DR FRANK C COMBES There is a remote possibility that this is not erythema induratum, but from a clinical standpoint I cannot favor any other diagnosis I will admit that this disease has its inception in the subcutis, but, as I understand it, the histologic section conformed to the changes seen in erythema induratum Because of its typical clinical features, I would agree with the diagnosis as presented, even if the histologic picture did not support it

DR TIMOTHY J RIORDAN I believe that is an adequate description, and the condition can be interpreted as Bazin's disease After all, the pathologic changes can be tuberculoid or tuberculous One does depend on the deep site of the biopsy material, and all that is necessary is to find changes in the region of the deep cutis, the region of the deep plexus of blood vessels It is true that it is best to include adipose tissue However, if by chance enough of the deep corium is got to correspond with the description given tonight, I would certainly accept it as erythema induratum, or Bazin's disease In my experience with erythema induratum tubercle formation or an entirely tuberculoid type of reaction may be present Often the diagnosis can be made without the appearance of classic tubercles as we know them, with caseation necrosis or pure epithelioid structure Inflammatory changes plus involvement of the blood vessels, tuberculoid reaction plus blood vessel reaction, or tuberculous reaction plus blood vessel reaction can establish the diagnosis

DR ISADORE ROSEN I agree with those who believe, on clinical grounds, that this patient is suffering from Bazin's disease When lesions of this disease break down, they frequently resemble gummas, and even on microscopic examination it is difficult to distinguish them from lesions of syphilis

DR MAURICE J COSTELLO I do not know how far Dr Irgang expected us to go in taking a biopsy, but, as Dr Rosen just indicated, I have seen lesions of papulonecrotic tuberculid accompanied with lesions of typical erythema induratum in the same patient

A Case for Diagnosis (Erythema Induratum? Pressure Grooves on the Sides of the Legs) Presented by DR MAURICE J COSTELLO

Superficial Epitheliomatosis Presented by DR S IRGANG

C S, a white woman aged 55, is presented from Harlem Hospital with an asymptomatic eruption which was first noticed sixteen years ago This appeared as a single lesion on the left arm, followed two years later by another on the small of the back Other lesions developed slowly, so that at present they are on the back, left arm, left flank and face The majority of lesions on the right cheek are nevi

The eruption consists of dry, nonulcerated nodules and plaques The former are firm, smooth, elevated, mildly hyperpigmented and/or pinkish, glistening lesions varying in size from that of a pinhead to that of a split pea, while the latter consist of slightly infiltrated, superficial, well defined, pinkish or reddish, flat, slightly depressed, scaly lesions with pearly, threadlike borders and varying in size from that of a split pea to that of a dime Thirty-seven years ago the patient took orally a clear, liquid medication in drop dosage for nine months and again twenty-four years ago for a two week period On each occasion it was discontinued because of intolerance There are no cutaneous evidences of either arsenical hyperpigmentation or arsenical keratosis Histologic examination shows the typical picture of basal cell epithelioma

DISCUSSION

DR DAVID BLOOM This patient gives a history of having received drops for acne vulgaris at the age of 18, administered during a period of eight months This was probably arsenic, and I suspect that her epitheliomatosis is a result of the arsenic ingestion

DR SAMUEL M PECK We are not sure the patient received arsenic, and if one wishes to speculate on such a causal relationship, one would expect palmar and plantar keratoses A patient may take potassium arsenite solution (Fowler's solution) for no more than a few weeks or months, and twenty years later keratoses and epitheliomas may develop

DR HERMAN GOODMAN Hundreds of thousands of persons have been given potassium arsenite solution in increasing dosage from 1 drop to 15 drops or more, three times daily, with no great number of them having superficial epitheliomas Pharmacologically, arsenic is a producer of keratin, it has been an ingredient in certain applications to the scalp as a hair grower Before the era of roentgen ray treatment for psoriasis, arsenic was given to patients with that disease In a few of them epithelioma developed on the site of the psoriatic patches A search of the literature disclosed that Arthur Alexander in 1920 assembled 18 patients with carcinoma of the skin together with psoriasis Of these, the disease in 11 was considered as malignant degeneration of arsenical hyperkeratosis or arsenical carcinomas on a psoriatic basis In the remaining 7 the lesions were considered as psoriatic carcinomas

Arsenic does foster the proliferation of epithelium, it is a keratoplastic agency It may cause the overgrowth of epithelium recognized clinically and under the microscope as epithelioma

DR SAMUEL M PECK I still believe that one of the best therapeutic measures in the treatment of psoriasis is arsenic, given properly From the statistics of the incidence of epithelioma, one finds that most of the patients never received arsenic, unless food is a possible source Persons who have never been exposed to arsenic have just as much if not more epithelioma than those who have received moderate doses of potassium arsenite solution I do not mean that treatment should continue for twenty years Therefore, in presenting this case with arsenic as a possible

eradicating this keratosis The odor which has been mentioned is that observed from other patients with hyperkeratosis and vegetative dermatosis and is due to putrefaction in the sulci and crevices

DR ISADORE ROSEN As far as erythroderma ichthysiforme is concerned, the clinical features do not fit in with that disease, which is almost invariably of congenital origin I am unable to make an absolute diagnosis, but I would suggest the possibility of Darier's disease

DR PAUL GROSS It would be interesting to hear about the therapy which this patient received during her year of hospitalization

DR FRANK C COMBS At one time we entertained the same idea as the chairman—that the patient might have Darier's disease, but this was ruled out on histologic grounds The patient has received large doses of vitamin A more or less empirically More recently, we have treated her according to the suggestion of Dr Goldzieher that this dermatosis was a manifestation of some endocrine disturbance occurring during the menopause I am sorry Dr Goldzieher is not here tonight, but Dr Reiss will be able to explain the therapy administered during the last two months, which I think is more logical than the previous treatment

DR PAUL GROSS There were two features which seemed important in this case One was the tongue, which had a magenta color and was rather smooth in appearance Secondly, there was pronounced anemia, which apparently has not changed to any degree during a year of therapy In other words, we are dealing with a case of generalized exfoliative erythroderma associated with lesions of the mucous membrane and profound anemia Such cases may respond to intensive therapy with vitamin B complex and particularly folic acid The fact that the patient is a Puerto Rican further suggests dietary deficiency, since we know that many of these people avoid meat in their diet If nutritional therapy is ineffective, the diagnosis of pemphigus foliaceus could be entertained This disease seems to be more common in South American countries than in the United States

DR FREDERICK REISS I have seen the patient only during the last two months I do not believe that I can offer a definite diagnosis, but since the onset of the disease was associated with bullae, Dr Wise's suggestion of pemphigus is a possibility I was led to think, however, that the disease process could be ichthysiform erythroderma, since the wet type starts with blisters We also have to recognize the other form, the dry type without blisters This case definitely began with blister formation, which later turned into erythroderma with plantar and palmar hyperkeratosis Hyperhidrosis is emphasized by Brocq and subsequent observers as occurring in erythroderma ichthysiforme, with, at times, loss of hair and sometimes increased growth of hair and nail plates I would not say that this case fits into the description altogether, because, as the chairman emphasized, in most instances the condition is hereditary Apart from that, there are many features suggestive of erythroderma ichthysiforme, and one may consider this a tardive form

An interesting symptom which I believe led us to the present therapy with estrogens was the amenorrhea which began six years ago, which may have some relationship with the disturbed keratinization I think the majority of French observers have emphasized endocrine deficiency, either ovarian, thyroid or adrenal This patient shows a definite endocrinopathy, not only clinically but biochemically, since there is tremendously decreased excretion of 17-ketosteroids The normal should be 11 to 15 mg, whereas she excretes only 7 mg All in all, I think that there is definite indication of an endocrine deficiency, but I cannot offer a definite diagnosis

expect, but in closure of the lesion Another feature is the pronounced anemia The patient was hospitalized mainly because of the very low blood cell count—as low as 30 per cent and often 50 per cent of normal

Eczema Verrucosum of the Legs Presented by DR LEWIS A GOLDBERGER

A Case for Diagnosis (Pemphigus? Bullous Eruption Due to Drugs?) Presented by DR LEWIS A GOLDBERGER

Multiple Benign Cystic Epithelioma Presented by DR S IRGANG

O D, an 8 year old Negro boy, has an eruption which was first noticed on both lower eyelids about a year ago The eruption is generalized, symmetric and nonpruritic and consists of pinpoint-sized to pinhead-sized firm, smooth, discrete, slightly elevated, flesh-colored and mildly hyperpigmented lesions, showing no tendency toward grouping The circular hyperpigmented area below the right jaw represents the end result of a recent fungous infection The child's mother has a similar eruption limited to both lower eyelids Histologic examination of lesions from the chest and right lower eyelid show the features of multiple benign cystic epithelioma

DISCUSSION

DR DAVID BLOOM Such lesions as the patient presents on his body are frequently seen in Negroes Recent histologic examination in such a case showed keratosis pilaris, mild keratosis extending also between the follicles However, the lesions on the face of this patient suggest the diagnosis as presented I am therefore inclined to consider that this patient has two kinds of lesions

DR NATHAN SOBEL I think that perhaps another pathologist would describe the eruption as syringoma, because that is closely related to benign cystic epithelioma and they may even simulate each other (Ingels, A E Epithelioma Adenoides Cysticum with Features of Syringoma, ARCH DERMAT & SYPH **32** 75 [July] 1935) It is the first case I have seen in a child I have seen a number of patients with the generalized syringoma type, but those I have seen occurred later in life, in the twenties or thirties

DR S IRGANG I agree with Dr Rosen that this disease is relatively rare in male subjects and it does not occur in so young a person Clinically, the lesions on the lower eyelids resembled multiple benign cystic epithelioma, but the others simulated micropapular tuberculid Histologically the lesions on the chest had to be differentiated from syringocystoma, but the latter was ruled out because the cells were evidently derived from the basal cell layer

Herman Sharlit, M D, *Chairman*

Maurice J Costello, M D, *Secretary*

March 4, 1947

Fixed Eruption *Around the Mouth Due to Phenolphthalein* or Bubble Gum? Presented by DR WILLIAM CURTH

DISCUSSION

DR WILLIAM CURTH There are various ingredients in bubble gum—cane sugar, corn sugar, cornstarch, a trace of vanillin, coumarone resin, oil of orange as a flavoring and oil of cinnamon, which is the main flavor Oil of cinnamon

DISCUSSION

DR GEORGE M LEWIS The features in this case, both clinical and histologic, may be interpreted to fit into the syndrome known as eosinophilic granuloma The lesions at present have undergone involution to a certain degree, and a biopsy taken at this stage might show a mixed infiltrate and not a pure eosinophilic infiltration The development of urticaria-like lesions, with subsequent disappearance and deposition of pigment, is a picture reminiscent of a patient I presented before this Section (ARCH DERMAT & SYPH **49** 375 [May] 1944), as well as before the Manhattan Dermatologic Society (ARCH DERMAT & SYPH **48** 436 [Oct] 1943) It is interesting that our patient had a Trichophyton purpureum infection of the feet, and, from the observations of Dr Cormia and myself, this case would seem to bear an etiologic relationship Inspection of this patient's feet suggested a fungous infection While not all cases of periarteritis nodosa are fatal, the prognosis is not as good as with eosinophilic granuloma, so that it would appear important to attempt to decide the diagnosis in this case by studying more histologic sections

DR CHARLES WOLF This case is unusual, and the diagnosis is difficult I was particularly impressed with a large lesion over the right pectoralis muscle which had a polycyclic border and was infiltrated There was severe itching The patient had had hemorrhagic bullae, papules, macules and all varieties of lesions that fit in with a diagnosis of mycosis fungoides I think that she bears watching for further evidence of that disease

DR FRANK C COMBES I appreciate Dr Lewis' remarks, and if a fungous infection and hyperergy can be substantiated in this patient they may explain the periarteritis The bullae seen on the feet tonight were not there a week ago She has had recurrent bullae, however, not only on the soles but on other parts of all extremities Examination of the walls and the contents of the lesions did not reveal fungi I do not know what the results of the trichophytin test were Periarteritis nodosa does not seem to be the rare disease originally described with a mortality in excess of 90 per cent In 1937 a comparatively benign chronic form was described (Carol, W L L, and Prakken, J R *Acta dermat-venereol* **18** 102-118 [Feb] 1937), and we have seen several patients recently who might be considered to have this type If the disease is interpreted as an allergic manifestation, it might be the result of a mycotic infection I do not know Sensitization to Bacillus coli has been indicated in some previous reports This patient underwent a cholecystectomy in 1944, which may bear on the origin of her present disease There was no histologic evidence of dermatomyositis but extensive nodal periarteritis throughout the reticular layer of the dermis and in the hypodermis, accompanied with a notable perivascular infiltration consisting essentially of polymorphonuclear cells and eosinophils The constant high eosinophil count of the blood, ranging from 10 to 20 per cent, is indicative of hyperallergization I am not prepared to say whether this patient has early eosinophilic granuloma, as I have never observed an early case of this disease

A Case for Diagnosis (Epidermolysis Bullosa?) Presented by DR EMANUEL MUSKATBLIT

Palmar and Plantar Keratoses (Arsenical?) Presented by DR MAURICE J COSTELLO

appeared fused, with absence of intercellular bridges The nuclei were pale and irregular, but they were hyperchromic There was considerable edema Some cells were large and vacuolated, and in one area were seen cells resembling Paget cells The infiltration with lymphocytes was pronounced The basal layer was indistinct Mitosis was present

Potassium permanganate baths were prescribed Sulfapyridine, 0 5 Gm four times daily, was taken from October 1 to November 6 A slight improvement was noted after one week of treatment, but it then ceased Carbarsone, 0 25 Gm four times daily, was given from November 6 to December 8, with questionable improvement The administration of vitamin A, 200,000 units daily, was begun on December 4 and has continued up to the present, and vitamins in the form of a therapeutic formula have also been taken during this period By Jan 15, 1947, there was remarkable improvement of the lesions, and by February 10 only the pigmented residua were found

The patient refused surgical therapy for the penile lesion

DISCUSSION

Dr Beatrice M Kesten Tonight I think it would be difficult to confirm the diagnosis, but when we saw the patient in December it was one of the most typical examples of the Senear-Usher syndrome that we have encountered

Dr Fred Wise The concurrence of two different types of dermatosis in this patient is of particular interest The eruption on the trunk appears to conform to the Senear-Usher dermatosis, and the diagnosis of erythroplasia of the penis has been confirmed by the microscopic examination It is of course interesting to speculate on the possible pathogenic relation between the two eruptions

Dr Gerald F Machacek This patient was shown by me last October, and at that time there was present a typical Senear-Usher syndrome The lesions of the body followed the neoplastic lesion on the penis In fact, he had another neoplasm, for which he has been operated on several times—a papillary carcinoma of the bladder, with presumptive cure The histologic picture of the penile lesion was epithelioma in situ The other lesions at that time were typical

Dr J Gardner Hopkins I think Dr Vero was interested in presenting this case because of the patient's response to treatment We cannot be sure that the result is due to the treatment given, but the change in the appearance of this man has been striking It came after a course of carbarsone during which he had shown no visible improvement Dr Vero employed this particular therapy because of the more evident response to vitamin A in a somewhat similar case

Dr Frank Vero I cannot explain the rationale of vitamin A therapy and the result obtained I treated another patient with pemphigus (Senear-Usher type), a 76 year old patient who had had the disease for three years She had had day and night nurses and all kinds of therapy including penicillin, bismuth, iodides and vitamins, without results or with only a temporary improvement In September 1946 she had keratoderma of the feet and subungual hyperkeratosis I prescribed 100,000 units of vitamin A daily, and within three to four weeks all her lesions healed The patient is able to go out daily She has gained weight, and for the past two months my services have not been needed It is interesting that this patient has had a poor appetite all her life, so that her food had to be actually forced on her

confirms what Dr Chargin said, that one seldom if ever thinks of granuloma inguinale as having extragenital lesions, although I understand that the lesion in the first case ever described was extragenital I agree also with Dr Sobel I have seen several patients at Bellevue Hospital in whom the lesions began as enlarged inguinal lymph nodes, broke through the skin, and then took on the characteristics of granuloma inguinale in which Donovan bodies were found In this case Donovan bodies were found in the lesions on the neck and in the groin It would not surprise me if they could be found in the enlarged lymph node also, as suggested by Dr Bloom

A Case for Diagnosis (Lichen Planus) Presented by DR WILLIAM LEIFER

Actinomycosis Simulating an Abscess Presented by DR EMANUEL MUSKATBLIT

M A, a girl aged 17½, presents an inflammatory mass in the left mandibular area of three and a half months' duration The lesion is fluctuant and tender and discharges a grayish green, purulent material from its lower pole In October a decayed left lower molar was extracted Several weeks later a "lump" appeared which was believed to be an abscess This was incised and drained twice, with little evidence of healing The patient received ultraviolet irradiations for a while During the first week in January the cause of the disease was discovered when the granules in the pus were examined and the ray fungus of actinomycosis was seen in the fresh specimen as well as in the Gram stain Results of cultures have not yet been reported

To date the patient has received approximately 6,000,000 units of penicillin with noticeable improvement

DISCUSSION

DR NATHAN SOBEL I was interested in the improvement with penicillin I understand that while penicillin is effective in most cases, some cases prove resistant to this form of therapy

DR EMANUEL MUSKATBLIT The patient was hospitalized for a few days in one of the large hospitals, where the lesion was incised and drained, but it did not heal A few weeks later it was again incised and drained, and the patient was kept under observation for two and a half months, without any one's looking at a drop of pus under the microscope Regular surgical treatment did not have the regular effect, and there was a history of a bad tooth in addition

There is no scarring, no hardening and no typical sinuses It looks like an abscess It is confined to the skin and subcutaneous tissues, and there is no evidence of involvement of the deeper tissues Diagnosis from laboratory examination was surprisingly easy in this case Three weeks ago, every drop of pus, which could be obtained easily, showed the presence of granules which were visible in unstained preparations and also with the Gram stain The patient was given penicillin, 50,000 units every three hours, day and night 400,000 units per day She has now had 6,000,000 units or more During the last few days there has been considerable improvement The central area subsided and no more pus discharged—just a little serum and blood It is planned to continue until 10,000,000 units has been administered, and probably sulfadiazine and possibly potassium iodide will be given Roentgen therapy has been deferred because the dosage would have to be large, with high voltage, and because of the possibility of its producing radiodermatitis on the face

Almost the entire scalp is affected The skin presents a dull erythema, abundant scaling and crusting There are several small yellow crusts pierced by hair (scutula) and areas of atrophy with alopecia Hairs in the affected areas are dry, grayish and lusterless On the right thigh there is a small, round, erythematosquamous lesion with a minute yellow point in the center

On microscopic examination, hairs and crusts from the scalp contained Achorion schoenleini in abundance in the hair shaft and in scutula Scrapings from the focus on the right thigh showed one lanugo hair with the same fungi

The patient's mother was born in the United States Her father emigrated from Italy in 1920 There are two other children in the family A boy, aged 8, is free from infection In a girl, aged 2, a scaly lesion developed on the scalp two months ago Microscopic examination of hairs from this lesion showed fungi of favus



Fig 1—Favus of the scalp

DISCUSSION

DR MARION B SULZBERGER One must always bear favus in mind when seeing lesions of the scalp, even in patients of American birth. About twelve years ago I saw a telephone operator with favus of the scalp in mild form resembling dandruff or mild tinea amiantacea, with some involvement of several nails She was of American birth, and I do not think I would have thought of favus of the scalp if I had not examined the nails and recovered Achorion schoenleini She had been exchanging headpieces with the other girls at the telephone switchboard On questioning the mother of Dr Muskatblit's patient, I asked her if any members of the family showed signs of favus and she said there were none Then the girl herself volunteered the information that the father, who was born in Italy, had

causative agent, one should be cautious If, with the epitheliomas, there were typical hyperkeratoses on the palms and soles, and if, in addition, the patient had been taking potassium arsenite solution for many years, it would be more plausible to consider arsenic as a causative factor I would not hesitate to prescribe arsenic in lichen planus or psoriasis, because of the remote possibility of the development of epitheliomas Patients who have taken potassium arsenite solution for many, many years are those in whom keratoses and malignancy growths develop

DR MARION B SULZBERGER I do not agree with Dr Goodman that, because thousands of patients who take a drug have not had manifestations, the drug can be exonerated as a possible cause of trouble in a given case If that were a valid argument, one would conclude that the proved reactions from phenolphthalein, the barbiturates, antisyphilitic arsenicals, salicylates and the like were not due to those drugs because hundreds of thousands of persons have taken them with impunity I think it correct to start the other way around and ask how many persons with multiple benign epitheliomas have had therapy with arsenicals or exposure to arsenicals If one questions these patients carefully, one finds that a surprisingly large percentage have had exposure to inorganic arsenicals and an exceptional patient has had exposure to an organic arsenical The history of exposure in these cases is so high that it cannot be due to chance, so it is permissible to conclude that the lesions in some cases must be due in some way to arsenic I do not mean that all multiple superficial benign epitheliomas are due to arsenic But arsenic is not completely exonerated even in those cases without therapeutic exposure, because occult exposure is practically universal These lesions occur not only after larger amounts of the drug are given, but sometimes also after small amounts I agree with Dr Peck, on the other hand, that this is no reason for withholding a valuable drug Most of these conditions are benign, and the complications are rarely dangerous Moreover, the incidence of these disagreeable by-effects is very small, considering the large number of persons who have been exposed to arsenic Therefore, if arsenicals are valuable drugs, there is no reason for withholding them, provided that the indications are clearcut, even if it is established that benign epitheliomas are due to arsenic However, the dosage should be correct and no unnecessary risks taken Every patient receiving arsenic should be under constant medical supervision, and every prescription for arsenic should therefore be marked "no repeats"

DR DAVID BLOOM Years ago I presented from Bellevue Hospital the case of a woman who had received arsenic for psoriasis over a period of three years and in whom typical arsenical keratosis developed on the palms and soles with basal and prickle cell epitheliomas on the body

Granuloma Inguinale, Sickle Cell Anemia with Sickle Cell Ulcer of the Ankle Presented by DR SAMUEL M PECK

DISCUSSION

DR SAMUEL M PECK Here, instead of a thrombosed varicose vein and lack of a proper blood supply, there is actual thrombosis of a blood vessel due to sickle cell thrombi One of the methods of treatment I have tried which has resulted in fairly rapid improvement was keeping the patient in bed for months at a time, taking her blood serum and adding penicillin, and applying it locally as a dressing I allowed this to remain on for a period of four or five days before changing, and there was an amazing response, not only in the secondary infection as one would

not be overlooked I believe that the patient should receive roentgen ray epilation without delay The longer the process is allowed to go on, the more danger of further dissemination Roentgen ray treatment would appear safe in this case, although I do not believe a patient should have a third epilation without careful consideration I doubt if local therapy is worth attempting, and I would be against experimentation when we know that local therapy is not effective When

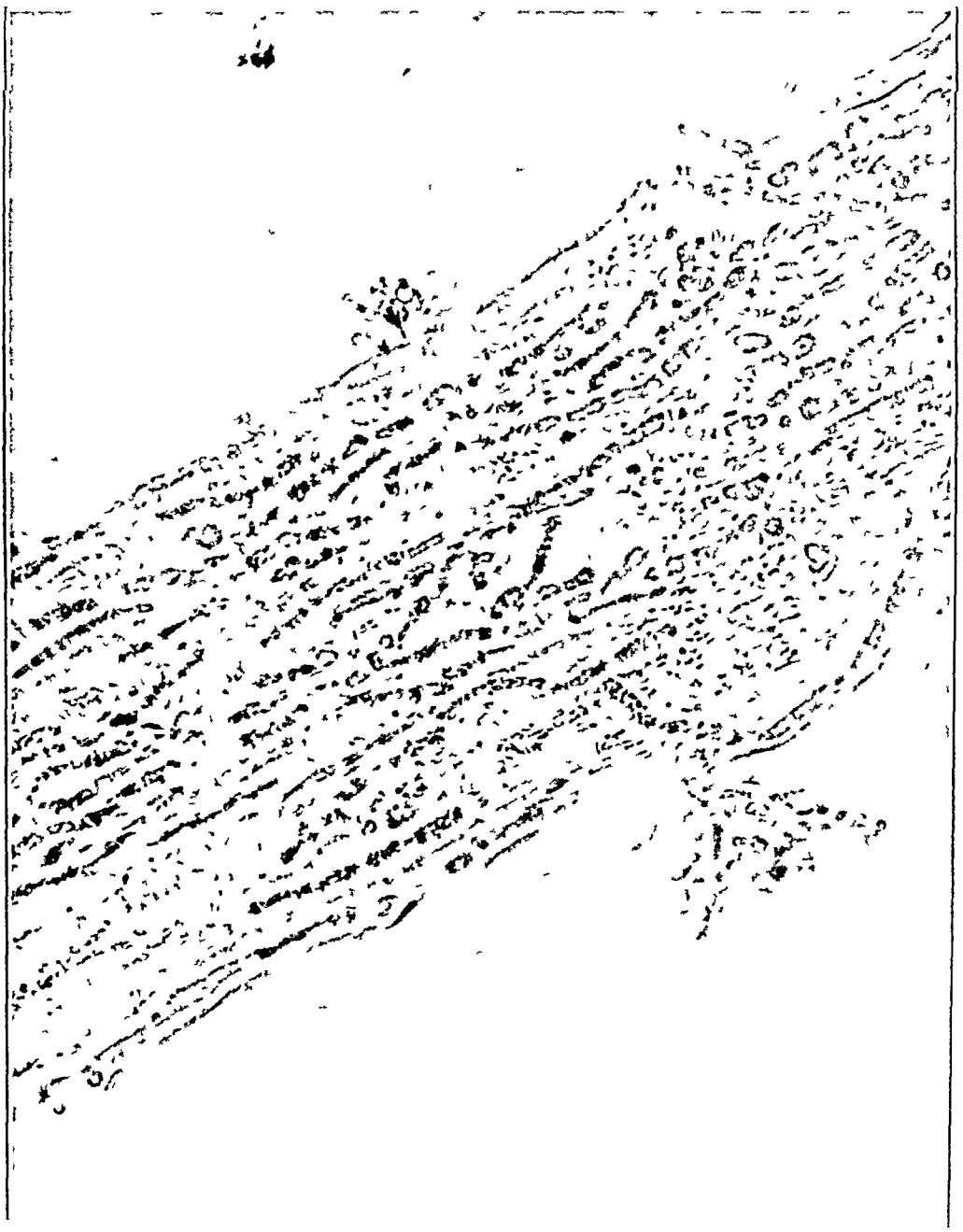


Fig 3—Achorion schoenleini in a lanugo hair from the thigh Potassium hydroxide preparation, × 770

I was examining this child, two of the younger men in the audience commented that they rather doubted the diagnosis because there were no scutula present I stated that we should censure Dr Muskatblit if the patient were presented with scutula The first step is to institute a good hygienic regimen to get rid of the bulk of crusts and scaling on the scalp before the roentgen rays are administered

has caused cheilitis in some cases, but there is no case on record of pigmentation or fixed eruption due to oil of cinnamon

Pemphigus Erythematosus (Senear-Usher Syndrome) Treated with Vitamin A, Erythroplasia of Queyrat Presented by Dr Frank Vero

J W, a Russian Jew aged 73, is presented from the Vanderbilt Clinic with an eruption on the face, trunk and extremities of sixteen months' duration and a lesion on the penis which has been present for five years

In 1944, after an attack of hematuria, a diagnosis of papillary carcinoma of the bladder was made It was treated by fulguration, and there has been no recurrence since September 1944 At that time a penile lesion was discovered, which had been present since 1942 This affected the glans, corona and sulcus

Late in 1945 small vesicles appeared on the sternum and quickly ruptured From then on, new lesions have appeared on the chest, arms, back and abdomen, and six months ago they spread to his face These lesions ruptured spontaneously, and soon became covered with a rather heavy, greasy scale He experienced little pruritus He denied the use of any drugs

Examination on admission showed dull erythematous patches, varying from 3 to 7 5 cm in diameter Intact bullae were present, these were about 1 cm in diameter and flaccid Most of the lesions were covered with gray-brown, greasy scales which were readily separable Heavy crusting was most apparent on the back and chest Two weeks later the small lesions on the right cheek had spread to cover both cheeks in butterfly shape A positive Nikolsky sign was elicited at this time on the patient's back On the glans penis, extending to the sulcus, there was a well defined, dull red, eroded and infiltrated lesion, measuring 1 5 by 2 cm, with a leukoplakic patch near the frenulum praeputii

A blood cell count showed 13 0 Gm of hemoglobin, 4,810,000 red blood cells and 7,500 white blood cells, with 68 polymorphonuclear leukocytes, 31 lymphocytes and 1 eosinophil

The serum cholesterol was 300 mg per hundred cubic centimeters and the serum protein 7 2 mg The albumin was 5 0 mg per hundred cubic centimeters, globulin 2 0 mg and nonprotein nitrogen 33 mg The cephalin flocculation test gave a negative reaction

Biopsy of material from the upper region of the right arm revealed a moderately xanthotic and edematous epidermis, with fairly prominent rete pegs in the central portion but with a flattened cutiepithelial line of juncture elsewhere No bullae or vesicles were seen in the section, but in their central portions were seen areas suggesting the "corps ronds," "grains" and space formation similar to those seen in Darier's disease, Hailey and Hailey's benign pemphigoid and pemphigus foliaceous The corium was edematous, particularly in the region of the pars papillaris, the capillary vessels were engorged and surrounded by a considerable perivascular infiltrate of round cells *In view of the clinical picture, it was felt* that a diagnosis of pemphigus erythematosus was justified

Biopsy of material from the prepuce showed an elongated, rectangular piece of tissue composed of loosely bound, fibromatous bundles, numerous blood vessels and lymphatic vessels and mucosa which presented a number of interesting changes in several areas There was an infiltration with lymphocytes, plasma cells and round cells in the subcutaneous tissues throughout their entire length, but it was most pronounced wherever the epithelium was thickened In such places the infiltration was massive The capillaries were numerous Where the epidermis was thickened there was also dyskeratosis The stratum granulosum was indistinct The most notable change was in the prickle cell layer Here the cells

tuberculosis At the beginning we were careful to duplicate exactly the steiogyl 15® preparations used by Charpy and others, who emphasized that it was essential to give vitamin D_2 in alcoholic solution We now think this may not be necessary as our patients treated with ertron,® davitol,® etc, do as well as those given the alcoholic solutions The American preparations just mentioned are readily available here, whereas the alcoholic solutions are not

Follicular Atrophoderma of Body and Scalp, Chondrodystrophia Calcificans Congenita Presented by DR HELEN O CURTH

Lupus Vulgaris Successfully Treated with Calciferol (Vitamin D_2) Presented by Dr MAURICE J COSTELLO

Sarcoid of Boeck Presented by DR S IRGANG

Epithelioma Presented by DR MAURICE J COSTELLO

M G, a woman aged 84 from Lenox Hill Hospital, presents a "browsing" type of basal cell epithelioma involving the forehead, cheeks and nose It consists of nodular, waxy, shiny, ulcerating, infiltrated strands of epitheliomatous tissue involving these areas There is some distortion of the nose, especially in the region of the right ala nasi This patient has received an incredible amount of roentgen rays according to the Coutard technic to a number of the affected areas on the face during the past six years Because of the age and infirmity of the patient, the treatment has been palliative

DISCUSSION

DR CHARLES WOLF I wonder whether there was not a previous disease here, later developing into epithelioma, for example, syphilis, although her Wassermann reaction may be negative at present Epithelioma does not generally extend the way this one has It is of the ulcerative type when it becomes so extensive This has the clinical appearance of the morphea-like or scleroderma-like epithelioma which generally follows a previous disease

Dermatitis Herpetiformis (?) with Mucous Membrane Involvement and Nail Changes Presented by DR FRANCES PASCHER

P R, a woman aged 42, born in Puerto Rico, is presented from the New York Skin and Cancer Unit complaining of recurrent attacks of "blisters" on the body and in the mouth for the past year These lesions are preceded by burning and pain The patient denies the ingestion of drugs

The patient presents a multiform eruption on the trunk made up of erythematous macular and urticarial lesions varying in size and shape There are also some thin-walled bullae on a noninflammatory base, with gyrate patches of pigmentation, atrophy and scarring There is a hypertrophic scar on the right shoulder Bullae followed by superficial ulceration also appear on the lateral edges of the tongue and buccal mucosa, and leukokeratotic changes are seen in the mouth The Nikolsky sign is strongly positive The nail changes include thinning and separation of the nail plate and subungual hyperkeratosis The neurologic examination is entirely normal

Biopsy of one of the bullous lesions showed a bullous eruption, with no definite diagnosis possible, and no defect in the elastic tissue Reactions to potassium iodide and potassium bromide were inconclusive, since the skin separated with the least

A Case for Diagnosis (Keratosis Pilaris? Lichen Scrofulosorum?) Presented by Dr F Philip Lowenfish

A Case for Diagnosis (Hemangiopericytoma?) Presented by Dr George C Andrews

J J M, an American student aged 18, first noticed a small "pimple" just inside his left naris about one year ago This tumor has continued to grow and is painless About five weeks ago his physician punctured the mass with a needle, which caused it to bleed a great deal

A single pea-sized, moderately firm, erythematous cystic nodule is present just within the left nasal orifice on the medial anterior aspect

The Wassermann reaction of the blood was negative, and the blood count was normal Biopsy has not yet been performed

DISCUSSION

Dr Charles Wolf These banal lesions are deceptive at times, the most innocent-looking lesions have turned out to be highly malignant In this case, I am of the opinion that it is a benign lesion I would favor granuloma pyogenicum

Dr Gerald F Machacek On the clinical basis, I agree with the diagnosis It is a site where hemangiopericytomas frequently occur Definite diagnosis must await examination of biopsy material

Dr Fred Wise The location and clinical appearance are in favor of the diagnosis of hemangiopericytoma A young boy seen at the Skin and Cancer Unit had a lentil-sized, slightly elevated, pinkish papule on the middle of the upper lip After complete desiccation it recurred and a tumor formed, spreading peripherally and into the deeper tissues It required an extensive radical operation on the upper lip, which I believe was performed by Dr Arthur Purdy Stout

Leprosy (Tuberculoid Type) in a Puerto Rican Man Aged 72 Presented by Dr A Benson Cannon for Dr Charles Lincoln

A Case for Diagnosis (Multiple Keloids? Dermatofibrosarcoma Protuberans [Hoffmann]?) Presented by Dr George C Andrews

Favus of the Scalp and Glabrous Skin Presented by Dr Emanuel Muskatblit

V V, a white girl aged 13, born in the United States and living in Belleville, N J, is presented from the New York University Skin Clinic

The disease of the scalp began four years ago with a scaly lesion which was diagnosed as psoriasis and treated with various ointments, ultraviolet irradiation and roentgen rays (eight roentgen ray treatments were given at weekly intervals from June to September 1946) The disease proved resistant to treatment and gradually progressed until it reached the present state During these four years the hairs from the scalp have been examined six times, and it has been reported each time that they did not show fungi The patient also had several red and scaly lesions on various parts of the body These lesions disappeared without treatment Only one focus, on the right thigh, has persisted for the last two months

DR A ROTTINO (by invitation) Yes, the clavicle is involved In no instance has the cutaneous involvement been primary, but it has been preceded by lymph node involvement The diagnosis in each case was established before the cutaneous lesions appeared

Kaposi's Sarcoma Presented by DR MAURICE J COSTELLO

A M, an Italian man aged 75, from the Lenox Hill Hospital Outpatient Department, in the early part of 1941 presented a soft, compressible, telangiectatic, marble-sized lesion on the right palm which was thought to be a pyogenic granuloma The lesion was destroyed by surgical diathermy but recurred with a number of satellite miniatures of the mother lesion Since that time numerous other lesions have appeared and are still present on the forearms, legs and thighs At present there are discrete, grouped, coalescing, purplish, globular, noncompressible, somewhat painful lesions on the legs and thighs, interfering to some extent with the venous circulation and causing brawny edema of the legs and feet There are a number of small warty excrescences on the dorsal aspect of the toes The axillary lymph nodes are enlarged Microscopic examination revealed the surface to be covered with stratified squamous epithelium surmounted by thick layers of keratinized, partially calcified material In a small area the surface epithelium was broken and missing Here and there exposed stroma showed fibroblastic proliferation and was rich in dilated small blood and lymph vessels A dense infiltration of inflammatory cells, chiefly round cells, was seen The electrocardiogram was normal

The disease has been well controlled with low, medium and high voltage roentgen rays The left palm received 1,000 r and the left axilla 1,200 r Two per cent sodium arsenate solution was administered by hypodermic injection at regular intervals, but was inferior to roentgen rays in therapeutic effect

DISCUSSION

DR DAVID BLOOM Two of my patients with Kaposi's sarcoma were treated with antireticular cytotoxic serum of Bogomolets but failed to respond

A Case for Diagnosis (Trophic Changes in the Legs and Feet Following Freezing) Presented by DR MAURICE J COSTELLO

Vaccination "Take," Left Index Finger Presented by DR TIMOTHY J RIORDAN

B D, a physician's office nurse, while assisting in numerous vaccinations two weeks ago, accidentally sustained a puncture wound from the virus capillary tube on the lateral aspect of the volar pad of the left index finger (fig 1)

Idiopathic Multiple Hemorrhagic Sarcoma (Kaposi) Presented by DR TIMOTHY J RIORDAN for DR ANTHONY ROTTINO

G M, a man aged 57, Italian, had Kaposi's disease for two and a half years Pathologic examination of a mass in the pharynx, lingual and tonsil area, removed in November 1946, and a biopsy of a cutaneous lesion, corroborated the diagnosis Treatment with seventy injections of nitrogen mustard was ineffectual

The patient was critically ill on admission to St Vincent's Hospital on Feb 25 1947, with evidence of ascites, gastrointestinal hemorrhage and peripheral

a deformed fingernail I think it would be worth investigating to find whether there is a focus there I hesitate to suggest any therapy on such scant evidence, but Dr Loeb at our clinic used a preparation called dermycin® (para-nitrophenol–sodium iodate solution) which had been submitted for trial He treated 1 patient with favus of the scalp which had recurred after two roentgen ray epilations



Fig 2—Achorion schoenleini in a scutulum from the scalp Potassium hydroxide preparation, × 300

with perfect results in a relatively short time Perhaps this preparation is worth trying in this case I shall be glad to see that Dr Muskatblit gets some dermycin® if he wishes to try it

Dr George M Lewis We had a patient a few years ago who had favus of the toe nail In the investigation of possible lesions in the family, the feet should

edema Roentgen examinations revealed intraluminal masses and obstruction On March 17 operation was performed in an attempt to relieve the obstruction and control the hemorrhage The patient died five days later

A Case for Diagnosis (Keratosis Blenorrhagica? Psoriasis?) Presented by DR MARION B SULZBERGER for CAPT C D BELL and DR LIONEL RUBIN

F G, a white man aged 22, first became ill in September 1946 At this time severe pain developed in the right hip, without apparent cause, which forced the patient to stop work This was shortly followed by similar pain in the right shoulder and scapular areas and on both sides of the chest He was then acutely ill, his temperature rising as high as 101 F in the afternoon The smaller joints of the extremities, including the wrists and ankles, also became painful In October the right great toe nail became tender and elevated, accompanied by pain and swelling of the dorsum of the foot The toe nail was removed by an osteopath, with no improvement At the same time the patient had iritis of the right eye, and he was now so ill that he was admitted to the United States Naval Hospital, St Albans N Y He had lost 30 pounds (14 Kg)

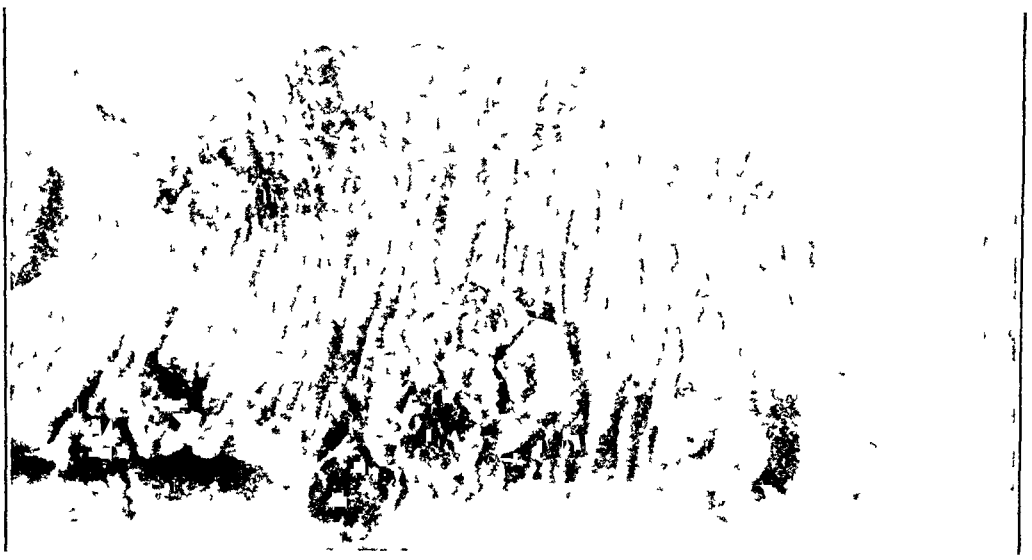


Fig 2—Gross pathologic specimen of intestinal section

The admission examination on November 18 revealed a dilated right pupil with posterior synechial pigment deposits on the lens and a cloudy aqueous blurring the fundus There were erosions on the tongue, buccal mucosa and palate and there was a discrete, papular eruption of the skin of the genitalia and inner aspect of the thighs "resembling scabies" The right scapula, left wrist, lumbar spine, right hip and right ankle were tender on pressure and painful on motion but exhibited no local heat, redness or swelling It was also noted that there was "an infected right great toe with associated cellulitis of the right foot" Otherwise the results of physical examination was normal, and, as the impression was that he had acute rheumatic fever, he was assigned to the medical service The erythrocyte sedimentation rate was 22 mm per hour, white blood cells 12,500 with polymorphonuclear leukocytes 73 per cent and lymphocytes 20 per cent, red blood cells, 4,300,000 and hemoglobin 12 5 Gm Blood cultures were negative

While on the medical service the patient continued to have a spiking afternoon temperature varying from 99 to 101 F The iritis cleared slowly with treatment, although some permanent dilatation of the pupil remained He received 6

DR EMANUEL MUSKATBLIT The scalp should, of course, be cleaned with some desquamating preparation to dissolve all scales and crusts and the hairs cut short, almost level with the skin, before epilation If scales, crusts and long hairs are left, we will not get the roentgen rays close enough The suggestion to examine the family is excellent It is possible that the father has favus of the nails As far as Dr Sulzberger's remark about trying a new chemical is concerned, I agree with Dr Lewis It would be pretty hard to try a new chemical in such an extensive case I should like to try it on the patient's sister, who has only a small patch I agree that roentgen therapy is now perfectly safe if we know definitely that no more than eight subfractional doses were given

Pigmented Nevus, Melanosis Oculi Presented by DR BEATRICE M KESTEN

Sarcoidosis with Enlarged Auricular and Cervical Lymph Nodes in a White Woman Aged 22 Presented by DR PAUL GROSS

Incontinentia Pigmenti in a Girl Aged 13 Months Presented by DR HELEN CURTH

Calcinosis of the Foot and Elbow with Normal Amounts of Calcium and Phosphatase in the Blood Presented by DR HELEN O CURTH

A Case for Diagnosis (Leprosy? Syphilis?) Involving a Negro Woman from the West Indies Presented by DR A BENSON CANNON

Parapsoriasis Guttata Presented by DR F PHILIP LOWENFISH

A Case for Diagnosis (Melanoma of the Leg, Multicentric and Pigmented Basal Cell Epithelioma?) Presented by DR FRANK VERO

George M Lewis, M D, *Chairman*

Marion B Sulzberger, M D, *Secretary*

May 6, 1947

A Case for Diagnosis (Lupus Erythematosus? Erythema Solare?) Presented by DR MAURICE J COSTELLO

Lupus Vulgaris Improved from Treatment with Calciferol (Vitamin D_2) Presented by DR FRANCES PASCHER and DR JESSE A TOLMACH

Lichenoid and Miliary Sarcoid (Boeck) in a Negro Woman Improved After Treatment with Calciferol (Vitamin D_2) Presented by DR MAURICE J COSTELLO

DISCUSSION

DR MARION B SULZBERGER We have overwhelming evidence from many countries, including the United States, that calciferol should not be withheld in any case of sarcoidosis, scoruloderma, tuberculosis colliquativa or other tuberculoderm, unless it is contraindicated Many cases of sarcoid appear to respond well to this treatment, which lends some support to the theory that it is a form of

At this point, Dr Lionel Rubin, consultant, suggested the use of estrogenic substance On April 3, diethylstilbestrol therapy was begun, he was given 0 5 mg daily, which was increased to 1 5 mg daily At the end of two weeks no new lesions were appearing and former lesions on the trunk were evident only as pigmented macules The mouth was clear Painful gynecomastia necessitated reduction of the dose of diethylstilbestrol to 1 0 mg daily on April 18 Improvement continued rapidly with respect to the cutaneous eruption, but no improvement of the arthritis was noticeable Roentgen reexamination on May 2 showed extensive demineralization of all osseous structures visualized, narrowing of involved joint spaces due to cartilaginous destruction and varying degrees of flexion and extension deformity Comparison of these roentgenograms with those of December 1946 revealed a fulminating type of rheumatoid arthritis

At present the patient exhibits loss of all finger nails, with hyperkeratosis of the nail bed, and an erythematous plaque on the dorsum of the right foot, which is slightly infiltrated The joint deformities persist in the fingers and toes, but the large joints are much less painful and motion is greater The patient has lost 70 pounds (32 Kg) during his illness Since April 17, the afternoon temperature has been less than 100 F

DISCUSSION

Dr E T Bernstein I think that the disease in this case is arthropathia psoriatica It seems to me that the nails and skin showed lesions of that disease

Dr Emory Ladany (by invitation) This case does not impress me as one of keratosis blenorrhagica for the following reasons In keratosis blenorrhagica there is gonorrhea This patient denies gonorrhea, and prostatic smear and cultures were negative It may be arthropathic psoriasis Since 1920, keratosis blenorrhagica has frequently been confused with arthropathic psoriasis In keratosis blenorrhagica, a urethral discharge precedes the arthritis, which is followed by the cutaneous lesions In arthropathic psoriasis there are first cutaneous lesions and then joint lesions In keratosis blenorrhagica the large joints are usually the ones involved and there is no distortion There may be a few cases with ankylosis of the involved joints, but this is rarely so Usually the arthritis is evanescent, whereas in arthropathic psoriasis the small joints are usually attacked and ankylosis and deformities are common The other diagnostic possibility is Reiter's disease, which has also been mixed up with keratosis blenorrhagica in the last decade or so This is a urethritis which is nonspecific, with arthritis and nonspecific conjunctivitis Ocular lesions are also common in keratosis blenorrhagica, and they have been reported exceptionally in arthropathic psoriasis Out of 47 cases of Reiter's disease reported, in only 13 were there cutaneous lesions, but without such great deformities of the nails and joints as in this case I reviewed 166 cases of keratosis blenorrhagica and also dealt with the differential diagnostic points of the two other diseases, and I believe that the disease in this case is arthropathic psoriasis

Capt C D Bell (by invitation) About a month ago this man's appearance was different than it is today At that time there was a generalized eruption, of which one now sees evidence in the form of pigmented macules on the trunk and upper extremities This was characterized as a vesiculopustule These lesions developed day after day, they started as vesicles, became pustular and then hyperkeratotic It is true that there is no gonorrhea On the other hand, the prostatic smear even today was loaded with pus cells, so that I think that there is fair evidence that at some time the patient did have a urinary disorder

trauma In three examinations of the blood the eosinophils did not exceed 10 per cent The bulla fluid was free of cells Results of serologic tests for syphilis were negative The urine was normal, and the basal metabolic rate was —11 per cent

Some improvement followed one course of treatment with potassium arsenite (Fowler's) solution, and a remission took place when therapy was discontinued Multiple vitamins have been taken three times daily over a period of months without apparent change Treatment with sulfapyridine is contemplated

DISCUSSION

DR FRANK VERO In spite of the biopsy, I think that a diagnosis of epidermolysis bullosa should be considered because of the nail changes, oral lesions and the atrophic changes and scarring on the back

DR DAVID BLOOM I believe that pemphigus should be considered, and onycholysis may be part of the eruption I do not recall having seen a case of dermatitis herpetiformis with such extensive eruption in the mouth

DR FRANCES PASCHER This patient presents a problem in differential diagnosis I do not know how one can say with finality what type of bullous eruption this might be, but I did consider all the bullous eruptions, such as epidermolysis bullosa, possible lichen planus and bullous Hansen's disease I considered the possibility of erythema multiforme bullosum, but this diagnosis was excluded because of the gyrate configuration of the patches, atrophy and pigmentation Most of the features fit in best with a diagnosis of dermatitis herpetiformis rather than the other eruptions

Hodgkin's Disease Treated with Nitrogen Mustard Presented by DR T J RIORDAN

E B, a man aged 20, is presented from St Vincent's Hospital In August 1945, there was enlargement of lymph nodes in the neck This was treated with roentgen rays In August 1946, a cluster of small papules appeared in the left axilla These persisted, grew progressively larger, coalesced and ulcerated Roentgen therapy had no effect In December, after nitrogen mustard therapy, the lesions regressed greatly In March 1947, the lesions again enlarged, reddened and drained Nitrogen mustard and roentgen therapy were again administered, and pronounced improvement followed, this has continued to date

DISCUSSION

DR A ROLLINO (by invitation) The usual cutaneous lesions observed in Hodgkin's disease are pigmentation, excoriations due to scratching and herpes zoster In a series of 75 cases of Hodgkin's disease my co-workers and I have encountered 3 patients with skin lesions similar to those demonstrated here, they appear in clusters of small nodules—in 2 cases on the chest and in the third in the axilla When the lesions first develop, they simulate pyoderma or a deep-seated vesicle They persist and may coalesce and ulcerate Biopsy establishes the diagnosis In the case demonstrated, roentgen therapy did not effect the lesion, but the response was spectacular to nitrogen mustard therapy The improvement lasted about three months, after which the lesions reappeared, grew larger and began to weep, itch and grow painful Again nitrogen mustard therapy was resorted to, and the lesions have almost cleared up

DR. DAVID BLOOM I should like to ask the presenter about the swellings of the right clavicle It seems to me there is involvement of the bone itself

Sporotrichosis Presented by DR TIMOTHY J RIORDAN

H W, a white man aged 50, born in the United States, is presented from St Vincent's Hospital The patient worked for two months repacking novelities shipped from Mexico in what is called "Mexican hay" In reshipping, this "hay" is mixed with excelsior On Jan 7, 1947, a thorn of cactus pricked the right middle finger The patient said that when he pulled out the thorn at least half an inch (1 cm) had been embedded under the nail plate He applied iodine Three days later he complained of a red, painful swelling He was cared for by a surgeon, and after four days of wet dressings the infected area was incised and

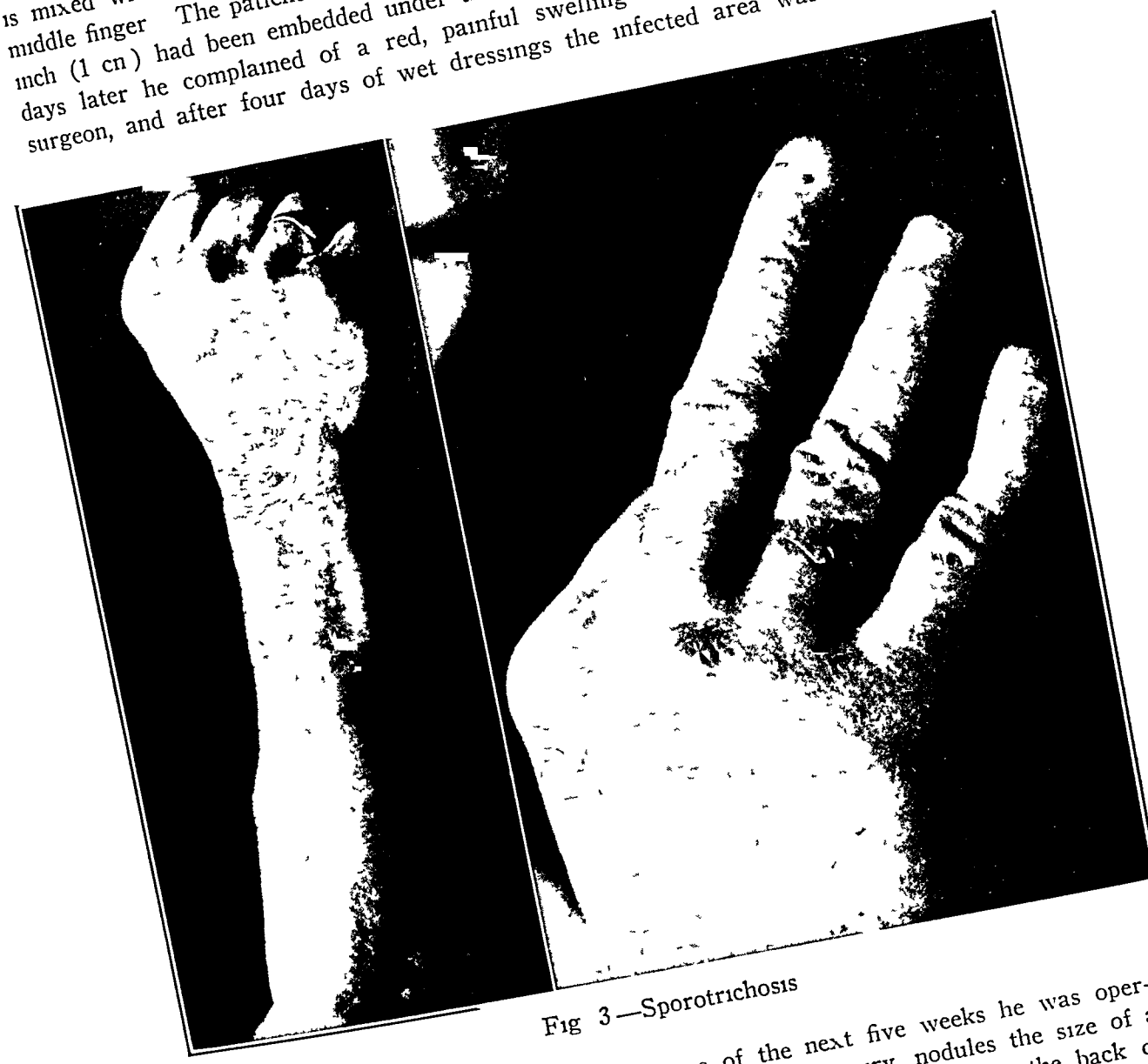


Fig 3—Sporotrichosis

the nail partially removed In the course of the next five weeks he was operated on four times Seven weeks after the date of injury, nodules the size of a pea and larger appeared, extending from the distal phalanx across the back of the hand and forearm to above the elbow These nodules were in linear arrangement, apparently following the course of the lymphatics They were dusky and firm, and subsequently one or two broke down Microscopic examination of the material discharged failed to reveal evidence of fungi Cultures from the nodules were positive, corroborating the diagnosis It is important to note that there was no enlargement of the epitrochlear or axillary lymph nodes Prior to the spread of the infection penicillin therapy was used without effect



Fig 1.—Vaccination "take" on the index finger

enlargement of the mediastinal nodes, because dilatation of the superficial cutaneous veins was a prominent feature, producing a caput medusae effect

DR WILBERT SACHS The patients that I have seen had not only generalized erythroderma but also severe itching Any such extensive eruption associated with prolonged itching may give a similar picture Some believe that the constant scratching results in the enlarged lymph nodes and that Symmers' disease is not an entity per se

DR EUGENE F TRAUB I am not sure whether the history stated whether the other lymphoblastomas, such as leukemia and mycosis fungoides, had been excluded, as the nodules in this case seem unusually firm I, too, have had the experience of seeing only generalized erythroderma in patients with this microscopic picture and have followed 1 case for approximately fifteen years, during which the patient had about three severe exacerbations and then the disease cleared up as a result of local therapy only It seemed to me that in these cases the lymph node involvement was secondary to that of the skin, but that does not seem to be the case in this patient, in whom the lymph nodes enlarged before the cutaneous lesions appeared Perhaps the presenter can tell us what has been done to exclude the other types of lymphoblastomas

DR ELSE A BARTHEL The condition in the biopsy specimen of the skin definitely resembled leukemia rather than a lymphoblastoma The appearance of the biopsy specimen of the lymph node was that of a lymphoblastoma Since the node reactions offer more of a diagnostic picture than the skin, it was thought preferable to accept the diagnosis based on the pathologic changes in the lymph node

DR FRANCES PASCHER The concept of giant follicular lymphadenopathy, or Brill-Symmers' disease, is still in an evolutionary phase It is now regarded by Craver and others at Memorial Hospital as "an early setting for lymphosarcoma" rather than a disease entity In 1938 Symmers pointed out that in some cases of universal chronic erythroderma there is local or general enlargement of the superficial lymph nodes with the histologic characteristic of giant follicular lymphadenopathy Similar histologic changes in the lymph nodes have also been described in association with other dermatoses Hurwitt *(J Invest Dermat, 1942)* stated that the benign follicular hyperplasia in the lymph nodes associated with dermatoses differs definitely from that in follicular lymphoblastoma He designated this benign follicular hyperplasia as dermatopathic lymphadenitis Differential diagnoses can be made only after careful study

My impression is that the patient presented has a follicular lymphoblastoma which has developed into a lymphosarcoma with cutaneous metastases The mediastinal nodes are not enlarged, and the blood cell count is normal

(NOTE—A lymph node was later excised, and the histologic report was lymphosarcoma)

Postvaccinal Erythema Multiforme Bullosum? Epidermolysis Bullosa? Presented by DR JOSEPH L MORSE

Multiple Superficial Basal Cell Epitheliomas Presented by DR JOSEPH L MORSE

M H, a woman aged 65, is presented from the Skin and Cancer Unit with a history of having taken potassium arsenite solution (Fowler's solution) at intervals for many years for the treatment of "eczema" The lesions first developed about thirty-five years ago, and since then new ones have continued to appear Many were treated years ago at the Vanderbilt Clinic with roentgen rays and radium

Gm of sulfadiazine daily for two weeks, followed by 6,000,000 units of penicillin intramuscularly, and boiled milk, but joint pain persisted and the cutaneous eruption gradually progressed He was first seen in consultation on the dermatologic service early in December, at which time a diagnosis of keratosis blenorrhagica was suggested and it was recommended that an investigation be made for a probable prostatic focus A genitourinary consultation disclosed no urethral discharge, shreds in the second specimen of a two glass test and a slightly boggy but not remarkably enlarged prostate, the secretion of which exhibited 50 white blood cells per high power field The patient consistently denied gonorrhea by name and symptoms He was given weekly prostatic massage and diathermy, and in January the urine was free of sediment and he had recovered from acute conjunctivitis of the left eye However, fever, tachycardia and joint pain persisted, with involvement of the right wrist and shoulder, onycholysis of all nails with hyperkeratosis of the bed and gradual extension of the skin eruption On Jan 11, 1947, the patient was seen in consultation by Dr Sulzberger, who suggested the possibility of an atypical psoriasis, the patient was transferred to the dermatologic service

The patient then received daily starch baths to macerate the heavy corneous lesions, followed by application of 50 per cent salicylic acid in petrolatum The fever, tachycardia and arthropathy continued unchanged, while a severe secondary anemia was now evident, the hemoglobin was 11 Gm, red blood cells 3,200,000, and white blood cells 8,200, with polymorphonuclear leukocytes 67, lymphocytes 25 and eosinophils 6 per cent Small transfusions of 250 cc of whole blood were administered with improvement

Biopsy revealed pronounced parakeratosis and acanthosis, migrating leukocytes in the rete processes and a heavy cellular infiltrate in the upper third of the corium The papillae were greatly elongated with thinning of the suprapapillary plates while the rete pegs were thickened, clubbed and fused These observations were felt to be consistent either with keratosis blenorrhagica or with psoriasis

The patient continued to show erosive lesions of the tongue and palate, but no vesicles were ever seen The original eruption on the genitalia had subsided, but on the lower extremities the lesions had tended to coalesce to form indurated, erythematous plaques in which the original papules could be distinguished The trunk, forearms, upper arms, nose and scalp were now involved by the process, and close study revealed that new lesions appeared first as apparent vesicles, perceptibly hard, which became pustular (cloudy) in about four days and then commenced to exhibit a tan, heaped-up, tenacious and hard crust The corneous exudate appeared to project through the skin, its base being surrounded by a slight erythematous halo Where formerly these hornlike excrescences had remained intact, they now yielded to the action of baths and salicylic acid and desquamated, leaving dime-sized, bright red papules These papules tended to coalesce to form the plaques previously described on the ankles

Prostatic secretion continued to show many pus cells Ointments of 10 per cent crude coal tar and 5 per cent ammoniated mercury had no effect, and the patient was then given bismuth sodium triglycollamate by mouth, beginning January 25, with 1 tablet (75 mg of bismuth) three times daily and increasing to 2 tablets (150 mg of bismuth) three times daily for a total equivalent of 9 7 Gm of bismuth No effect whatever was obtained On February 27 he was given potassium arsenite (Fowler's) solution by mouth, treatment commencing with 4 drops three times daily, gradually increasing to 7 drops three times daily and then decreasing to 4 drops again, for a total of 20 3 cc over a period of nineteen days Again no effect was evident

treatment for fear of sequelae which are irreversible, especially in the later decades of life Bone marrow activity is at a low ebb, and, therefore, administration of actinic rays is fraught with greater danger than when they are given to a younger skin I would therefore advise local excision as the better and safer procedure with so many lesions

DR JOSEPH L MORSE We all realize that arsenic has some relation to the production of basal cell epithelioma It is interesting that 2 such patients should be encountered at one meeting, one showing arsenical keratoses and the other not, but both with a history of ingestion of potassium arsenite solution, and it seems more than a coincidence that in both patients epitheliomas should have developed I have treated some of these lesions, and I think that they can be easily destroyed by electrodesiccation and curettage, certainly with better cosmetic results than this woman shows, and at the same time with no chance of radiation sequelae

Allergic Eczematous Cross Sensitization to Paraphenylendiamine and Several Azo-Dyes Certified for Use in Foods, Drugs and Cosmetics (Contamination of an Innocent Cosmetic with Paraphenylendiamine.)

Presented by DR RUDOLF L BAER and DR MORRIS LEIDER

S B, a woman aged 38, a worker in leather sundries, presented an eczematous eruption on the hands, arms, back and chest of eight months' duration Initial patch tests with a series of common eczematogenic allergens revealed a strongly positive (3 plus) reaction to paraphenylendiamine With this lead, additional tests were done, with the results noted in table 1

At this presentation the patient exhibits the results of patch tests applied forty-eight hours ago (table 2)

DISCUSSION

DR BEATRICE M KESTEN There is a crisscross sensitivity to adhesive tape I am not impressed by the cutaneous reaction to a test to nylon This woman wears nylon stockings, and she has no dermatitis on the legs I wonder whether she is so cross sensitive The results of patch tests as seen tonight do not exhibit it Perhaps she is sensitive to some of the ingredients in adhesive tape, and it might be well to test that possibility Instead of incriminating the numerous substances of which Dr Baer speaks, it might be that the patient is sensitive to paraphenylendiamine, a substance with which she comes in contact and to which she gives a positive reaction in patch tests

DR MARION B SULZBERGER If it can be shown that there are cases of cross sensitization between ordinary certified food dyes and other dyes commonly encountered in objects which come in contact with the skin from without, this might have a most important bearing on the difficulty of clearing up certain eczematous dermatoses when one has removed the offending external dye allergens Such refractoriness could perhaps be caused by relatives of the dyes being encountered in foods Moreover, it is possible that some eczematous or fixed eruptions which were reported as due to foods were really due to the dyes in these foods Because of the far reaching importance of these observations, I would again ask the presenter whether he considers the patch test reactions, as seen tonight, significant? I am inclined to agree with Dr Kesten that the patient tonight does not show any unequivocal reactions to nylon-dyes or other dyes

DR RUDOLF L BAER I agree with Dr Kesten and Dr Sulzberger that the test results in this patient are poor examples for demonstration I observed that several such "certified" azo dyes produced more strongly positive reactions in a

DR LIONEL C RUBIN (by invitation) This patient gives no history of gonorrhea, but, as Dr Bell stated, he has chronic prostatitis, before studies for bacteria were made he had already received 5,000,000 units of penicillin, so that may have prevented isolation of the Gonococcus In this case the joint changes preceded the cutaneous eruption by months In psoriasis it is the reverse Also, the cutaneous lesions were originally vesicles and pustules, becoming hyperkeratotic, of the waxy type, which is characteristic of keratosis blenorrhagica, and he had lesions in the mouth He has a history of iritis That would be difficult to fit in with psoriasis, but it would fit in well with gonorrhea He had a severe constitutional reaction, with pronounced loss of weight and a swinging temperature Why was there no response to penicillin? Such cases have been reported in the literature, and I think that Dr Ladany's patient had positive evidence of gonorrheal urethritis, yet the rash and joint pains did not respond to penicillin therapy There has been great improvement in the last two weeks I do not know whether that is coincidental or whether it was due to the diethylstilbestrol therapy Every type of therapy had previously been tried without improvement, and diethylstilbestrol was suggested because of the rarity of this condition in female subjects After the patient had received diethylstilbestrol, gynecomastia developed, he began to improve, and practically all the cutaneous lesions disappeared

DR LOUIS TULIPAN I believe that this is a case of psoriasis arthropathica In this disease hyperkeratotic lesions are prone to develop, especially on the palms and soles, plus pronounced subungual keratosis In gonorrheal arthritis one expects a monarticular involvement This man has a multiarticular involvement He has a generalized eruption on the body, which coincides with a superficial type of psoriasis, and shows fairly typical plaques I do not believe that arthropathic psoriasis can be ruled out simply because the arthritis preceded the eruption, or vice versa I feel that it is a case of psoriasis arthropathica

DR WILLIAM CURTH Was a complement fixation test for gonorrhea performed?

DR RUDOLPH L BAER Besides the complement fixation test for gonorrhea, it might be worth while to try a new procedure recently described, which might help to differentiate the present eruption from Reiter's disease In the Scandinavian literature (Storm-Mathisen, A *Acta dermat-venereol* **26** 547, 1946) is described a skin test for Reiter's disease using as test material tissue emulsions and joint exudate from a patient with "known" Reiter's disease

DR LOUIS TULIPAN I would also suggest that this man might have received medication for his arthritis—one of the sulfonamide drugs or some other drug—and that the vesicular-pustular eruption which developed all over the body may have been a reaction to that or to the penicillin Such eruptions frequently terminate in the guttate or nummular form of psoriasis

DR MARION B SULZBERGER The discussion shows that this is still a case for diagnosis I would put arthropathic psoriasis first with a question mark, keratosis blenorrhagica with two question marks second and Reiter's disease with three question marks third I have seen 3 cases almost identical to this one, and the same discussion followed in each instance One thing was not mentioned In the one biopsy, the histologic picture was characteristic of psoriasis The patient is beginning to improve since receiving diethylstilbestrol Dr Rubin is to be complimented Even though it is not yet certain that this estrogen has cured the patient, it would surely be well worth while to treat other patients with that preparation The similar case Dr Baer and I reported and depicted (Sulzberger, M B, and Baer, R L Yearbook of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc 1944, pp 202-203) terminated fatally

DR RUDOLF L BAER It is possible that some of the occupational materials had contaminated the old jar of deodorant cream However, it is conceivable that certified azo dyes contained in the nail polish might have been responsible

Lupus Vulgaris (Treated with Calciferol). Presented by DR MARION B SULZBERGER

A S, a woman aged 33, was previously presented at the New York Dermatological Society, on Oct 24, 1939 She is shown tonight to illustrate the good results of calciferol (crystalline vitamin D_2) therapy and the simpler dosage schedule employed

In 1924 the patient first noted an eruption on the right cheek consisting of small erythematous and tumid nodules which healed with central whitish depressed scars The eruption gradually spread to involve the entire right cheek, chin, nose, forehead and both lips Previous treatment included radium, roentgen rays, electrodesiccation, tuberculin, Kromayer lamp, generalized ultraviolet irradiation and gold sodium thiosulfate, given by various dermatologists and clinics, with no great improvement

On May 3, 1946, vitamins A and D_2 (100,000 units of each daily) were given, in addition to tuberculin and ultraviolet irradiation On October 4, all other treatment was discontinued and the patient was given ertron® (concentrated vitamin D preparation) capsules daily (50,000 units) plus calcium lactate (4 0 Gm daily) Since that time she has shown gradual, consistent and finally great improvement No new nodules have appeared, and there has been no peripheral spread The skin has become less erythematous and has assumed a more normal color In addition, it has been more flexible, and the patient stated that there is increased mobility of the circumoral tissues especially, which previously interfered with mastication and speaking

Lupus Vulgaris, Improved with Calciferol Therapy Presented by DR JACK WOLF

V T, a man aged 47, is presented from the New York Skin and Cancer Unit with an eruption in the left postauricular region of approximately fifteen years' duration He was born in Italy and has lived in the United States for the past twenty years The eruption has never been troublesome, and the patient presented himself only recently because of the gradual extension of the process

He presents an erythematous, well marginated, brownish red patch involving the posterior auricular region and extending on to the temporal and mastoid regions The lobe of the ear is involved, and well developed small nodules are present in this location The process has improved greatly since calciferol therapy was instituted about four weeks ago, the nodular lesions have regressed considerably

The Wassermann reaction of the blood was negative, and the urine revealed no abnormalities There was no reaction to the intradermal tests with tuberculin in dilutions of 1 100,000 and 1 10,000

A histologic report by Dr A Hyman stated that in the upper part of the cutis there were groups of epithelioid and giant cells in tubercle arrangement There was a banal infiltrate around the tubercles

DISCUSSION

DR MAURICE J COSTELLO Calciferol is a good medicament for lupus vulgaris I have also treated patients with generalized lichenoid sarcoid with calciferol with equally good results and think that it is worth a trial in this dermatosis also

The patient was given sodium iodide, 1 Gm daily the first week and every other day thereafter, with potassium iodide by mouth He has responded well, and eruption is almost clear, but there is still evidence of nail changes and residual nodules are present on the forearm

This is the first compensation case of sporotrichosis in the state of New York

NOTE.—One year later the patient was completely cured

George M Lewis, M D, *Chairman*

Marion B Sulzberger, M D, Secretary

Nov 5, 1947

Follicular Lymphoblastoma Presented by DR FRANCES PASCHER

H R, a man aged 44, complains of lymphadenopathy of three years' duration A node was excised for histologic examination from the right axillary chain two years ago There has been no palpable change in the size or consistency of the nodes during the three months in which the patient has been under observation A red patch appeared near the left temple one year ago A few weeks later a similar lesion appeared near the right temple The patient has lost about 10 pounds (4 5 Kg) during the past three years He has been well enough to work but does not feel as energetic as formerly

There is a well defined plaque of erythema and infiltration in both preauricular areas The nodes in all superficial chains are enlarged The liver and spleen are not palpable

A biopsy specimen was taken from the right temple on August 8 The section showed masses of cells not surrounded by any inflammatory exudate The collagen fibers within the lesion were edematous and broken The cellular exudate consisted of small round cells containing highly pigmented nucleoli There were no eosinophils or mitotic multinucleated cells The diagnosis was lymphoblastoma

The section taken from the lymph node was examined by Dr M Richter, and the diagnosis was malignant lymphoma, follicular type

A roentgenogram of the chest revealed no abnormalities Scout roentgenograms of the abdomen showed a slightly prominent liver and spleen Study of the sternal marrow was attempted, but a suitable specimen could not be obtained Three complete blood counts were normal, as were the results of urinalysis The Wassermann reaction of the blood was negative

DISCUSSION

DR DAVID BLOOM Years ago I saw all the patients for whom this diagnosis was made at Bellevue Hospital All the patients showed universal erythroderma with pronounced enlargement of the lymph nodes This patient shows only a few circumscribed cutaneous lesions in association with generalized adenopathy The diagnosis as presented should therefore be questioned

DR GERALD F MACHACEK I have seen several patients without erythroderma and without glandular involvement—1 with the lesions localized, 1 more diffuse and both of them evidently cured by total excision Reexcision was necessary for 1 a year after the first operation, but ultimately the entire disease process was eliminated and the patient cured

DR MAURICE J COSTELLO I should like to confirm what Dr Bloom said, that all patients observed during the time Dr Symmers was making his studies of this disease had generalized or universal erythroderma I cannot recall a case in which the eruption was limited to a small area I think that the patient must have

and shoulders Vesicular encrusted lesions in plaques are seen in arciform arrangement with active borders and clearing center The old lesions seem to have left depigmented areas The Nikolsky sign can be elicited near the lesions

Results of serologic tests for syphilis were negative, the urine was normal, and no fungi could be found in scrapings The report of biopsy by Dr Charles Sims was Hailey-Hailey disease

The patient is married and has no children He does not know whether either of his parents or his brother or sister had a similar condition

DISCUSSION

DR ARTHUR B HYMAN It was suggested that this might be tertiary syphilis because of the configuration of the lesions, but they are crusted and bullous and there is a positive Nikolsky sign There is some clinical similarity to dermatitis herpetiformis, but the eruption does not itch The patient said that he has had it for six years The unusual feature is the fact that, if his story is correct, the eruption developed at the age of 67 No cases have been reported in which the disease developed as late as that Most cases are familial, but such a history was not elicited from this man His parents died years ago, and his siblings live far away, so that he would not know about the state of their skin Fortunately, the histologic picture in Hailey-Hailey disease is characteristic

DR GERALD F MACHACEK I treated a patient with a similar condition, and the patient improved with large doses of vitamin A, the improvement lasting over a period of months I do not know the ultimate outcome

As a matter of fact, the problem is older than when the Haileys posed it McCarty, in his "Histopathology of Skin Disease," wrote of these peculiar cases which have some characteristics of pemphigus and some of Darier's disease

DR WILBERT SACHS I was surprised to hear Dr Hyman call this Hailey-Hailey disease In our article my co-workers and I decided that this is a variant of epidermolysis bullosa

DR ARTHUR B HYMAN (by invitation) Whether it be epidermolysis bullosa or not, this eruption was described by Hailey and Hailey, and therefore there is no discrepancy

The lesions in Hailey-Hailey disease are found on the sides of the neck, axillas and groins with a degree of symmetry, and there is usually a familial history The disease lasts many years with frequent remissions One can generally exclude other possibilities, such as tinea by mycologic examination, syphilis and other diseases, by careful analysis of history, lesions and symptoms The histologic aspect of this disease is characteristic, and the only other eruption for which it could be mistaken at a quick glance under the microscope is Darier's disease, but in the latter one always finds corps ronds and grains In Hailey-Hailey's disease the lacunas are characteristic and are found just above the basal cell layer, corps rond are not found, and grains are rare

Sarcoid, with Results of Kveim Test Presented by DR JESSE A TOLMACH

E L, an Italian woman aged 39, is presented from the New York Skin and Cancer Unit with an eruption of six years' duration Nearly the entire scalp is involved with scaly erythematous flat patches Around the right ear and toward the back of the neck there are several pea-sized papules of light yellow-orange On the left side of the face, right arm and right thigh there are indurated telangiectatic coin-sized plaques The past history is not relevant

The patient now has several discrete crusted lesions on the forehead, sides of the cheeks, back and abdomen and small superficial erythematous macules scattered on the trunk and extremities There are several whitish atrophic scars and telangiectatic atrophic areas on the forehead, cheeks, abdomen and thighs Numerous keratoses are present on the back and abdomen The palms and soles are free of lesions

A report of biopsy of a lesion on the abdomen was basal cell epithelioma

Multiple Superficial Basal Cell Epitheliomas with Arsenical Keratoses

Presented by Dr Jack Wolf

C B, a man aged 60, was previously presented before the Manhattan Dermatological Society on Oct 14, 1947, with multiple lesions on the trunk and legs of about twenty years' duration

DISCUSSION

Dr Eugene F Traub This type of case is not uncommon, and one sees some who have taken arsenic and others who have not A relationship to psoriasis has also been observed, or, at least, patients have been seen in whom the multiple epitheliomas were perhaps mistaken for psoriasis, in others, psoriasis had been treated with arsenic and later multiple superficial epitheliomas developed In 1 case, the multiple epitheliomas had been mistaken for tinea and in a laboratory fungi were found in each of the lesions This in itself should have made any observer suspicious, because fungi are not found so readily in every lesion It is not known exactly how arsenic influences or brings about these lesions or just what the effect of sunlight may be A great deal has been said about treatment, and it has been said that the lesions are sometimes more difficult to cure than the ordinary basal cell lesion on the face This has not been my experience, as improvement occurs with desiccation and curettement, either with or without roentgen therapy, and sometimes a sufficiently large dose of roentgen rays clears up the early lesions also

Dr Joseph L Morse What is the consensus as to treatment?

Dr J Gardner Hopkins I believe that roentgen rays are effective in this type of basal cell epithelioma Atrophy does occur in the area, but it is not a particularly threatening type In desiccating lesions on the trunk one is apt to see secondary infections My inclination would be to treat these lesions with roentgen rays first and then use desiccation for recalcitrant areas

Dr Wilbert Sachs The patient has different types of lesions seborrheic dermatitis, lesions similar to Bowen's disease, superficial basal cell epitheliomas and arsenical keratoses on the palms The lesions on the lower extremities are basal cell epitheliomas, corroborated by the microscopic observations The quantity of radiation necessary to destroy lesions which have been present for twenty to thirty years is large, and such therapy is rather radical However, such lesions occasionally do become active and heroic methods are needed

Dr David Bloom I have had occasion to observe patients with psoriasis who took organic arsenic and had arsenical keratoses on the palms and soles and, in addition, basal cell epitheliomas on the trunk and squamous cell epitheliomas on the extremities I believe that in this case there is a causal relationship between the ingestion of arsenic and the development of epitheliomas

Dr Charles Wolf These cases illustrate the fact that disseminated epitheliomas are always caused by drugs or actinic exposure Fortunately, in these cases the history is straightforward One does encounter cases in which the patient denies taking arsenic, but it must be remembered that it may be ingested in an occult way, as through the food or occupation As to therapy, I feel that where there are so many lesions on the body it is inadvisable to give radium or roentgen

NEW YORK DERMATOLOGICAL SOCIETY

George C Andrews, M D, *President*

George M Lewis, M D, *Secretary*

March 26, 1946

Axillary Hidradenitis Suppurativa, Pyoderma, Cystic Acne in a Girl Aged 15 Presented by Dr Fred Wise

Nevus Cerebriformis Presented by Dr Fred Wise

B G, a single girl aged 18, in good general health, presented a birthmark involving the skin of the posterior and external lateral surfaces of the right thigh It extended from the gluteal fold down to about one third the length of the thigh, it was roughly rounded in outline, with well defined borders and was approximately 8 inches (20 cm) in diameter In addition to the primary growth, there were a few scattered satellite, pea-sized nodules at a distance from the main lesion The tumor consisted of groups of soft, light brown, partly pedunculated and partly sessile nodules, some of which exhibited cerebriform and cauliflower-like surfaces, while others consisted of yellowish white, rounded, easily compressible "lumps" resembling superficial deposits of fatty tissue, covered with clinically normal skin

The birthmark produced a pronounced degree of disfigurement of the affected region, the patient was presented for the purpose of obtaining advise as to therapy

DISCUSSION

Dr. Howard Fox I would do nothing at all for this lesion It is fortunate that it is not situated on the face, neck or arms To perform an extensive skin graft would be ridiculous, as the lesion does not bother the patient in the slightest degree

Dr. Eugene F Traub The lesion in this case is too extensive in my opinion for surgical intervention Furthermore, since the lesion is a spreading and extending one, I feel sure that it would certainly promptly appear beyond the line of surgical excision This in itself would be most distressing to the patient and would, in my opinion, argue against surgical removal Superficial desiccation, on the other hand, could be carried out on each of the lesions, and, because of the large amount of intervening skin between the patches, this would strike me as being the treatment of choice Microscopic examination of one of the lesions would prove that this is probably a benign type of growth, and, if the desiccation is carried out properly, it could be done with safety and great improvement to the patient

Dr A Benson Cannon I agree with Dr Fox This lesion should be untreated, but, should treatment be demanded, it might be possible to remove the lesion in successive steps, leaving only a linear scar eventually

Dr. George M MacKee I suggest leaving the lesion alone, or else complete excision, with plastic repair I know of several instances in which epithelioma developed in this variety of nevus after it had been severely traumatized with solid carbon dioxide

number of patients with paraphenylendiamine hypersensitivity than in a series of "normal" control subjects Some of these dyes have primary irritant properties on human skin

There are many azo dyes that are certified by the Food and Drug Administration for use in food, drugs and cosmetics and others which are certified for use only in drugs and cosmetics Those azo dyes which were tested in this patient are certified for all three uses Their use is widespread, they can be encountered in such diverse products as nail polish, sausage casings, raspberry syrup and other beverages

We do not know yet what is the clinical importance of these reactions It is possible that these cross sensitizations to azo dyes may account for some of the chronicity in cases of dermatitis due to paraphenylendiamine, and perhaps also for

TABLE 1 —*Results of Tests*

Test Substance	Reading	Source of Contact
Black suede leather	1 2 plus	Occupational
Rubber glove	3 plus	Therapeutic
Black satin dress	3 plus	Wardrobe
Brown dress A	1 2 plus	Wardrobe
Brown dress B	2 plus	Wardrobe
Navy blue dress	2 plus	Wardrobe
"Fresh" deodorant (old jar)	2 plus	Cosmetic
"Fresh" deodorant (new jar)	Negative	Cosmetic

TABLE 2 —*Results of Additional Tests*

Test Substance	Reading	Potential Source
Paraphenylendiamine	4 plus	Fur dyes, hair dyes, etc
Red No 1 *	Negative	Foods, drugs, cosmetics
Red No 2 *	Negative	Foods, drugs, cosmetics
Red No 3 *	Negative	Foods, drugs, cosmetics
Red No 4 *	Negative	Foods, drugs, cosmetics
Red No 32 *	Negative	Foods, drugs, cosmetics
Yellow No 3 *	2 plus	Foods, drugs, cosmetics
Yellow No 4 *	2 plus	Foods, drugs, cosmetics
Yellow No 5 *	Negative	Foods, drugs, cosmetics
Yellow No 6 *	Negative	Foods, drugs, cosmetics
Orange No 1 *	Negative	Foods, drugs, cosmetics
Orange No 2 *	Negative	Foods, drugs, cosmetics
Nylon stocking	2 plus	Wardrobe

* Food drug and cosmetic dyes

some of the unexplainable flare-ups This particular patient showed a very mild reaction to tests with the dyed nylon stockings In most cases of paraphenylendiamine hypersensitivity, reactions to nylon stockings containing these azo dyes are much stronger However, the fact that the patient gives a positive reaction in a patch test but does not have a stocking dermatitis is not surprising, because even in cases of dermatitis due to dyes in nylon stockings, with strongly positive reactions, the entire leg is usually not involved In most cases only the dorsa of the feet and the popliteal spaces are involved, showing that the eruption tends to develop in sites where maximal extraction is likely to occur

As far as the deodorant cream is concerned, it is possible that the patient contaminated it with the nail polish, which may contain one of the azo dyes

DR EUEGNE F TRAUB Why was the deodorant considered to be contaminated by nail polish rather than by paraphenylendiamine?

necrosis of the newborn The duration and age of the patient is against it A malignant melanoma may develop in this infant

DR ANTHONY C CIPOLLARO I do not believe that there is any fatty necrosis here I do not believe that this shows any lipomatous tissue I think that it is a mass of nevus cells I feel, as do most of us here, that the lesion should not be treated and that nothing can be done for the child, I agree with Dr Cannon that it is a relatively benign type of lesion

Mycosis Fungoides. Presented by DR FRED WISE

Chronic Lichenoid Discoid Dermatitis, Arrested; Dermatophytosis, Erythroplasia Presented by DR A BENSON CANNON

Universal Scaling Erythroderma Presented by DR HOWARD FOX

L S, a man aged 62, a dress shop owner, first noticed an eruption ten years ago It began on his legs and within six years had become universal The eruption is red, scaly, dry and nonpruritic In each axilla there are two partly fused, firm lymph nodes, the size of a pigeon's egg and a hen's egg, respectively

Laboratory examinations showed a faint trace of albumin in the urine The Kline and Mazzini reactions of the blood were negative A blood examination on Nov 10, 1944, showed 6,500 leukocytes, with 52 per cent polymorphonuclear neutrophils, 44 per cent lymphocytes and 2 per cent eosinophils A second blood examination, on March 7, 1946, showed essentially normal observations, except for 12 per cent monocytes

A biopsy specimen taken on Feb 1, 1946, was examined by Dr Wilbert Sachs, who made a microscopic diagnosis of tuberculosis cutis His report was as follows Throughout the middle and upper parts of the cutis there is a diffuse intense cellular infiltration composed of wandering connective tissue cells, small round cells, occasional plasma cells and many epithelial giant cells, the latter arranged in tubercle formation The overlying epidermis is irregularly acanthotic Part of the basal cell margin is washed out and part is intact There is some parakeratosis No lepra organisms were found

Four years ago, and again one year ago, the patient was operated on for inguinal herma, on each occasion by a different surgeon Both operations were failures and were followed by large elephantiasic masses in the upper third of the thighs On one of these occasions, an inguinal (or femoral?) node was excised and examined microscopically It was said to have shown nonspecific adenitis

The patient appeared to be in fairly good general health He never takes drugs, including vitamins He has had a good deal of roentgen treatment without any benefit, which would tend to exclude either psoriasis or mycosis fungoides

DISCUSSION

DR FRED WISE Generalized tuberculous erythroderma was described by Jadassohn (Volk, R Tuberkulose der Haut, in Jadassohn, I Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927 vol 10, pt 1, p 420)

DR FRANCIS PASCHER We now have 9 or 10 patients at the Skin and Cancer Unit who have been treated with calciferol for lupus vulgaris for approximately six months to one year About 75 to 80 per cent improvement is attained in about six to eight months of treatment, and then progress is much slower, or seems to come to a standstill The problem of how to treat the residua presents itself

DR ANTHONY C CIPOLLARO Calciferol certainly is not a cure-all for cutaneous tuberculosis, but it is the best remedy that dermatologists have ever had to combat this disease, as well as lupus erythematosus and other tuberculodermas It is also interesting to note that calciferol is derived from irradiated vegetable ergosterol and so is related to ultraviolet irradiation Up to the present the only effective treatment for lupus vulgaris has been ultraviolet irradiation, especially as carried out at the Finsen Institute at Copenhagen Now there is a remedy derived through the action of ultraviolet irradiation on ergosterol

DR RUDOLF L BAER In connection with the superficial nodules remaining after treatment with calciferol, Lomholt has recently advised a combination of calciferol and Finsen treatment Apparently the deep nodules cannot be reached by the Finsen treatment, and the superficial ones cannot be reached by calciferol He believes that the combined treatment may solve the problem

DR CHARLES WOLF One must always be on the lookout for atheromas of the capillaries of the kidney especially, and also of the smaller vessels of the myocardium Patients given calciferol and calcium should have frequent determinations of the blood calcium Where there are residua, an ointment containing 3 per cent calciferol is effective

DR MARION B SULZBERGER The answers to most of the questions asked are to be found in the recent literature At the New York Skin and Cancer Unit we used dosage schedules of 600,000 units, three times for the first week, twice for the second, third and fourth weeks and once weekly thereafter because we think it essential to work along the exact lines a predecessor has followed, to repeat as accurately as possible what was done originally, in order to see whether we obtain the same results as the original observer So we went to great pains to use the same doses and preparations as Charpy, getting the solutions of sterogyle 15® (vitamin D preparation) from France and treating our patients in the same way as was done there Then, having fully confirmed what earlier observers have said, we then used other preparations of vitamin D_2 and used modified dosage schedules I would hazard a guess that the optimum dosage might be different in each case, as with gold compounds and the arsenicals I think that the future and fundamental study of this form of treatment is important We know that this vitamin schedule is effective in some cases of sarcoidosis Is that an added argument in favor of the thesis that sarcoid is some form of tuberculous infection, or is vitamin D_2 (calciferol) also good for other types of granulomas not due to tubercle bacilli? If so, it might be good for tuberculoid leprosy, and many other important granulomatous infections At my suggestion, Dr Wade is planning to try it out in the tuberculoid and lepromatous forms of leprosy Will vitamin D_2 be valuable in treatment of any types of tuberculosis of the viscera, and if so, which forms? These and many other questions can be answered only when many investigators take up and extend this new form of treatment introduced by European dermatologists

Chronic Benign Familial Dermatosis (Hailey-Hailey) Presented by DR NATHAN SOBEL

R M, a man aged 72, is presented from the New York Skin and Cancer Unit with a rash which has been present intermittently for six years It started on the left side of the neck and now involves the dorsum of the chest, sides of the neck

left Incidentally, this boy had a pigmented hairy nevus on the forehead, near the hair margin One of the patches of depigmentation involves this nevus, which is rapidly losing its pigment as a result.

DR A BENSON CANNON This is totally unlike any vitiligo that I have ever seen The linear rim around the white area is raised, red and firm, and the depigmented center is most likely the result of previous inflammation I think that we shall have to depend on the histologic examination for the diagnosis The raised lichenoid margin somewhat resembles lichen planus

DR FRED WISE It is interesting to call attention to the fact that a similar case was reported by Becker and Obermeyer (ARCH DERMAT & SYPH **36** 216 [July] 1937, and **37** 99 [Jan] 1938) Today the border is less elevated than when it was seen in the clinic, about two weeks ago Another interesting fact is that the patient has typical vitiligo of the penis and scattered vitiligo on other parts of the body, there are no signs of lichen planus and no signs of a border on the other lesions

A Case for Diagnosis (Poikiloderma? Localized Scleroderma?) Presented for DR GEORGE C ANDREWS by DR A BENSON CANNON

Neurodermatitis with Cataract and Asthma Presented by DR FRED WISE

F S, a young man aged 17, registered at the Skin and Cancer Unit on March 19, 1946, presenting lesions since infancy He has also been suffering with asthma since then The asthmatic attacks have been mild for the past several years The cataract in the left eye formed about three years ago He has five brothers and sisters who are well A cousin of his mother has asthma and had eczema The patient had chickenpox, German measles, scarlet fever, whooping cough and pneumonia in childhood and appendicitis at the age of 13 His general health has been good He complains of itching

The patient presents an almost perfectly symmetric and extensive eruption on the lower half of the forehead, face, front of the neck and upper and lower extremities On the face the lesions are distributed on the lower half of the cheeks, with the chin comparatively free On the upper extremities they commence just above the elbows, envelop the arms and end on the volar surfaces at the wrists, but include the dorsal surfaces, the hands and the terminal phalanx of the right middle finger The lesions are most pronounced on the lower extremities and encircle almost completely and uninterruptedly, except for the inner and upper surfaces of the thighs, the thighs and legs down to the distal half of the dorsal surfaces of the feet, terminating in a sharp margin They consist of heavily crusted oozing vesicular fissured patches, infiltrated and thickened to several millimeters The soles are hyperkeratotic, particularly the heels and the anterior metatarsal arches The back is uninvolved except for isolated spots On the chest, elbows and arms are fairly numerous pinpoint-sized to pinhead-sized, irregular, dry crusted patches on the back of the scalp In the groins the lymph nodes are enlarged to the size of goose eggs and in the axillas to cherry size

NOTE —The patient is hospitalized at the New York Post-Graduate Hospital Laboratory reports will be given later

DISCUSSION

DR GEORGE M MACKEE It is important, for medicolegal reasons, to know that spontaneous cataracts occur in this disease, otherwise roentgen treatment is likely to be unjustly blamed, as has not infrequently happened

Results of serologic tests for syphilis were negative The urine and blood cell count were normal The tuberculin reaction was negative in a dilution of 1 100 A roentgenogram of the chest showed perhaps slight engorgement of the superior great vessels There was a slight degree of lymphoid nodulation at the hilus and root devoid of definite etiologic characteristics There was moderate generalized hypervascularity No evidence of recent parenchymatous infiltration was seen The report of biopsy was sarcoid The result of the Kveim test was negative after nine days, with the Oslo antigen With the Copenhagen antigen it appeared to be 1 plus after three days and 1 to 2 plus after seven days

DISCUSSION

DR DAVID BLOOM The patient shows typical sarcoid lesions on the back of the neck, but the other lesions are flat and not infiltrated Together with the lesions on the scalp, they form an extraordinary feature in this case

observed two types of reaction caused by penicillin in sycosis, some patients showing a great increase in pustules and inflammation after its local use for a few days and others an acute vesicular outbreak with much redness and discomfort within forty-eight hours after its first application

I have used quinolor® in sycosis plus roentgenotherapy, 75 r once a week, with such satisfactory results that this method is used by me almost exclusively

DR MAURICE J COSTELLO I think that the best treatment for these cases is compound quinolor® ointment, and, if properly rubbed in three times daily, before and after shaving and at night, it is effective

DR JOHN C GRAHAM I have had poor results with penicillin in the treatment of sycosis vulgaris I have had better results with compound quinolor® ointment, but have had few permanent cures

DR FRED WISE I share the views of those who favor manual epilation, it is one of the most important methods of therapy The patient should be taught not to pull the skin out with the hair and to allow his beard to grow for two or three days I feel that some of these cases are almost incurable A fluid preparation known as intraderm® (antifungal agent) combined with tyrothricin is of considerable value in the treatment of this disease

DR EUGENE F TRAUB This patient has had much treatment, but the best remedy for so severe a condition has not as yet been used, and I see no reason why a careful roentgen epilation should not be done It has been my practice to do this in the bearded area, using a divided dose and alternating with ultraviolet rays from a cold quartz lamp to control and prevent a pustular flare-up This has always been successful, and the patient is free of eruption in approximately six weeks from the date of the first treatment I believe that the aftercare from this point on is also extremely important because there is a tendency to relapse Therefore, while the new hair is growing back, I usually have the patient use either quinolor® ointment, ammoniated mercury or some other similar mildly antiseptic cream If the new hair is kept free of infection, the patient is permanently cured

DR A BENSON CANNON Any case of folliculitis is difficult to cure While manual epilation is the method of choice in treating localized areas, in cases with generalized sycosis, it is almost impossible and certainly impractical to pull out all the hairs About a year ago I presented a patient with generalized sycosis of several years' duration who was cured with wet dressings and injections of penicillin and frequent potassium permanganate baths I had 3 cases of generalized sycosis cured with this treatment within three to six months

DR GEORGE M LEWIS In order to obtain maximum results from penicillin applied locally, some individualization in the strength of the application is desirable Cormia has found tests of sensitivity to the bacteria found in culture to be helpful in gaging the concentration of the penicillin to be used Empirically, one may use higher percentages of penicillin when the response is poor to standard strengths

DR GEORGE C ANDREWS I was impressed by the apparently infected lower teeth All the upper teeth have been pulled out The patient never had roentgenograms taken of his lower teeth His gums are retracted and show definite gingivitis, and I suspect that he has root abscesses I agree with those who prefer manual epilation and quinolor® ointment If sulfonamide drugs were not

Universal Scaling Erythroderma Presented by DR HOWARD FOX

Lichen Sclerosis et Atrophicus, Accompanied with a Bullous Eruption Involving Vitiliginous Areas of the Vulva and Anus Presented by DR MAURICE J COSTELLO

Dermatitis Herpetiformis Refractory to Treatment with Sulfonamide Drugs Presented by DR MAURICE J COSTELLO

Nevus Pigmentosus et Pilosus Presented by DR ANTHONY C CIPOLLARO

D W, aged 2 months, was first seen on March 21, 1946, because of an extensive nevus involving the major portion of the body The father and mother have no similar lesions, and there is one other child in the family, who is well The pediatrician informed the parents of the possibility of cancer developing in these lesions and of the possibility that the child may grow up with mental defects

The patient now presents a lesion which is black and thick, and involves the bathing trunk area and halfway up the trunk There is hair in all parts of the lesion On other portions of the body are isolated black or brown pigmented hairy lesions

DISCUSSION

DR HOWARD FOX This case of bathing trunk nevus is not the typical brown hairy type The pigment is rather dark, almost black, and, in addition, there are other defects There is nothing that can be done for this child

DR A BENSON CANNON I believe that this is a benign type of lesion

DR EUGENE F TRAUB There are two types of nevi present in this case One, an ordinary brownish black, pigmented lesion with some slight fine downy hair, and the other, a deeper-seated bluish black or slate black mass It is possible, therefore, that there are a blue nevus and an associate nevus of another type, possibly a junction To further complicate the picture, there are some nodular masses underlying several of the bluish lesions, and they may be part of the bluish nevus, or they may perhaps represent areas of subcutaneous fat necrosis of the newborn The child is just a few months old, and the masses have been present since directly after birth As subcutaneous fat necrosis of the newborn is a self-limited process and usually clears up in a month or two, keeping this patient under observation will settle the diagnosis without the need of a biopsy

DR FRED WISE Is it the consensus of the members that the nevus be untreated?

DR HOWARD FOX None of the patients with subcutaneous fat necrosis that I have studied had pigmentation like this, and there always was a definite hardness which this child does not have In subcutaneous fat necrosis of the newborn, the skin is practically normal in color The location of the disease is also different from that in this patient

DR MAURICE J COSTELLO I think that the masses represent the fibrolipomas rather frequently observed in this type of pigmented hairy nevus I agree with Dr Fox that there is nothing in these tumors to suggest subcutaneous fat

DISCUSSION

DR HENRY E MICHELSON (by Invitation) I was glad to have the opportunity of seeing this patient I agree with the diagnosis of Schaumann's disease, and I think that some common term should be used for all of these sarcoid conditions, like sarcoidosis I think that this disease is a general condition, not necessarily a system disease, for the various systems most commonly involved are the lymph nodes, skin, lungs and bones However, even the meninges may be involved There is still much studying to be done on the subject It is strange that the Scandinavians see so much in their country and here the disease is seen so commonly in Negroes I feel that one should take a broad view of this disease, have an open mind as to causation and not expect the histologic picture to be as precise as has been believed in the past The course of sarcoidosis is variable some patients having complete remissions and some having the disease for many years

DR. MAURICE J COSTELLO I think that the herpes zoster in this case is an interesting feature and that it is due to pressure on the posterior nerve roots by the lesion of this disease A similar mechanism occurs in Hodgkin's disease

DR. ANTHONY C CIPOLLARO It is my understanding that in a number of these cases pulmonary and even miliary tuberculosis develops later

DR FRED WISE I am grateful for this discussion, from which I have gained considerable knowledge The only point against the established diagnosis of Schaumann's disease is the absence of uveitis perhaps the process is not sufficiently advanced to have caused this symptom I have in mind fever therapy for this patient

A Case for Diagnosis (Annular Atrophic Lichen Planus? Scleroderma?). Presented by DR FRED WISE

Epidermolysis Bullosa, Spina Bifida Occulta, Vitamin Deficiency Associated with Ichthyosis Presented by DR A BENSON CANNON

A Case for Diagnosis (Sarcoid? Granuloma Annulare?) Presented by DR. FRED WISE

Epidermolysis Bullosa Confined to the Palms and Soles Presented by DR MAURICE J COSTELLO

L C, a girl aged 19, has had recurring large thick-walled painful bullae on the bearing surface of the feet and on the palms since she was 3 years of age The eruption on the soles is present mainly in the spring and summer, when she is more inclined to walk Blisters occur on the palms at points of pressure after such household duties as ironing clothes In addition, she presents a number of calluses on the pressure points of the dorsal aspect of the toes There is some redness and scaling of the dorsal aspect of the last phalanx of the fingers The feet have an aged appearance Yesterday it was observed that, in addition, the patient complains of chapping, redness and scaling of the lower third, anterior surface of the legs and the tip of the nose in cold and windy weather Treatment has been palliative, consisting of rupturing the vesicle and use of potassium permanganate foot baths

DR GERALD F MACHACEK In the sections one finds microscopic evidence of the formation of tubercles I am, however, not certain that from this evidence alone one should accept the diagnosis of tuberculosis cutis Not so long ago I saw a similar case, that of a young person suffering from exfoliative dermatitis for many years Microscopic examination of sections from his skin showed not dissimilar tuberculoid infiltrations, but I was able to show to my own satisfaction that they were foreign body reactions to epidermal inclusions Others have reported and I have seen "tubercles" in cutaneous lesions of leukemia

DR HOWARD FOX I may say that the patient has no evidence of tuberculosis as far as I can find out He is perfectly well and has no itching, the only peculiar fact is the surgical reaction which he had on two successive occasions after herniorraphy

Squamous Cell Epithelioma, Grade 3 Presented by DR JOHN C GRAHAM

Juvenile Acanthosis Nigricans Presented by DR FRED WISE

Vitiligo with an Elevated Border Presented by DR FRED WISE

A L, a boy aged 13, registered at the Skin and Cancer Unit on Feb 26, 1946, presenting depigmented patches of two months' duration A vitiliginous spot first appeared on the penis, about one to two weeks later a spot appeared on the forehead, two weeks later on the left eyebrow and a month later on the left side of the forehead at the hair margin

The patient presents depigmented white patches on the forehead, left side of the neck, left eyebrow, shoulder and penis They vary in size from 1 to 3 cm The depigmented spot on the left side of the forehead is round, of silver dollar size and encircled by an evenly, slightly raised, threadlike border In the middle of the forehead is a blackish, depigmented, half-dollar-sized, round spot, which has been present since birth, surrounded by a depigmented zone of 0 5 cm The results of the routine laboratory tests were normal

From a section taken from the depigmented patch with the raised border Dr Charles F Sims made the diagnosis of superficial exudative inflammatory process The description follows The epidermis is slightly irregular Its surface is covered in part by a very mild, loosely laminated horny layer At several points the granular layer has all but disappeared The basal margin is pigmented throughout one portion of the section and relatively nonpigmented in the remaining portion There are scattered chromatophores The rete pegs are somewhat irregular, and at some points of the basal layer liquefaction has taken place At the latter point there is a mild cellular reaction composed for the most part of small round cells The vessels of the upper part of the corium are moderately dilated and surrounded by a sparse cellular reaction composed for the most part of small round cells Numerous vacuoles apparently due to edema are present at several points in the corium

DISCUSSION

DR EUGENE F TRAUB A similar case was presented at the American Dermatologic Association, Inc, meeting in Chicago about two years ago I do not recall exactly how the peculiar border was explained, except that there may be some inflammatory process at work and with the peripheral extension of this inflammatory and slightly elevated border an area of depigmentation is

reactions of the blood and the spinal fluid were both 4 plus on April 16 The patient has received 4,000,000 units of penicillin, 100,000 units every three hours

DISCUSSION

DR RAY H RULISON It is rather curious that, in a person obviously with neurosyphilis and with Argyle Robertson pupils, there should be such an extensive syphilitic eruption as this Cutaneous eruptions are relatively rare in neurosyphilis How would this eruption be classified, assuming it to be a syphilitic eruption?

DR A BENSON CANNON One frequently sees involvement of the nervous system in cases of early syphilis and especially in the late secondary stage This patient's cutaneous lesions have greatly improved with penicillin

NOTE—The diagnosis from biopsy of the cutaneous lesion was syphilis All lesions disappeared after the penicillin injections

Acanthosis Nigricans Presented by DR FRED WISE

A S, a boy aged 12, registered at the Skin and Cancer Unit on April 16, 1946, presenting cutaneous lesions of eight months' duration He has two brothers, aged 5½ and 3½ years, who do not have any cutaneous disease He had measles, chickenpox, scarlet fever, German measles and mumps during childhood and a streptococcic infection of the throat and recurrent infections of the left ear His appendix was removed at the age of 10 He was also subject to mild attacks of hay fever His maternal grandmother died at the age of 56 from a tumor of the kidney which became polycystic The paternal grandmother had a kidney removed "for some ailment," and two years later the other kidney became affected and she died at 52 The paternal uncle died at 35 after a kidney removal Both grandfathers died of "heart attacks" Obesity is a familial trait Most of the members of the family from the grandparents down have been and are obese

The mother stated that the child's neck was always darker than the rest of the body, and this was thought to be due to exposure to the sun The boy is of average intelligence He feels strong and well, except for occasional attacks of frontal headaches

A "sore" area first developed on the right side of the neck, this would clear up for a week or two and then recur after he wore rayon shirts or used soap When he avoided rayon shirts and soaps the soreness would regress, leaving rough areas which would become rougher after each attack of soreness Two months later the patches began to spread around the neck The pigmentation in the axillas appeared at the same time as those on the neck The patch on the left cubital region developed about two months ago

Examination shows blackish pigmentation on the neck, axillas and left cubital region The neck shows black dry nontender somewhat infiltrated patches which are irregular in outline, ill defined and intermingled with depigmented patches They feel rough, like sand paper The pigmented areas blend gradually into the surrounding integument There are similar symmetric patches in both axillas, blackish brown, and well defined, silver dollar-sized, dull brownish patch in the

DR MAURICE J COSTELLO I had a patient who had received a great deal of roentgen rays (from another physician) to the face, and even though the eyes were covered with lead protectors bilateral cataracts developed The ophthalmologist attributed the cataracts to the roentgen ray therapy until he was informed of the association of juvenile cataracts with neurodermatitis He had never heard of spontaneous cataracts forming in young persons with the dermatosis and had always thought that they were caused by roentgen rays This is of medicolegal importance

George C Andrews, M D, *President*

George M Lewis, M D, *Secretary*

April 23, 1946

Sycosis Vulgaris Presented by DR HOWARD FOX

C V W, aged 38, a guard by occupation, was discharged from the Army five years ago, after three years of service During the last fourteen months in the Army he was constantly receiving treatment in various hospitals He now presents an eruption confined to the upper lip and entire bearded area, which was previously of pustular type and now resembles a scaling eczema

Treatment in Army hospitals consisted chiefly of penicillin, roentgen rays and ultraviolet irradiation He received an enormous amount of penicillin, administered both by intramuscular injections and as an ointment He received a total of three hundred and fifty injections, in three courses of treatment, which completely failed to influence the eruption He also had seven fractional doses of roentgen rays (without causing epilation) at the Walter Reed Hospital, after which he was practically well for two months The disease then recurred in the same severe form He was at one time given general and local ultraviolet radiation for six weeks, which was followed by a deep tan on the body, but had no effect on the eruption On another occasion, he used quinolor® ointment (contains 10 per cent benzoyl peroxide and 0 5 per cent quinolor® [a mixture of three chlorine derivatives of 8-hydroxyquinoline] in a base of equal parts of petrolatum and wool fat) in various strengths for two weeks with slight benefit The patient appears to be in good general health and is again working full time He was first seen by me on April 1, 1946, and since then he has used quinolor® ointment once a day with slight improvement

DISCUSSION

DR ANTHONY C CIPOLLARO Cases of sycosis vulgaris tax the resourcefulness of the dermatologist I find that manual epilation of infected hairs is effective Tyrothricin, penicillin and other new antiseptics in easily absorbable bases, combined with injections of toxoid and small weekly doses of roentgen rays improve or keep under control most cases of sycosis vulgaris I certainly oppose the use of roentgen rays for the purpose of producing permanent epilation

DR PAUL E BECHET I believe that the local use of penicillin in sycosis vulgaris should be discontinued if no improvement occurs after it has been applied for a week, as cutaneous reactions from penicillin are, in my experience, greatly increasing in number—so much so as to become almost commonplace I have

Eugene F Traub, M D, *President*
George M Lewis, M D, *Secretary*
Nov 26, 1946

Lupus Erythematosus Presented by DR ANTHONY C CIPOLLARO

R P, a boy aged 3, was first seen by me on Nov 15, 1946, with an eruption on the face which the mother thought followed mosquito bites The eruption appeared on both cheeks and finally spread across the nose After about two weeks the child was taken to the Skin and Cancer Unit, where a blood cell count, tuberculin tests and a biopsy were performed

The blood cell count showed mild secondary anemia The reactions to tuberculin tests were negative in dilutions of 1 1,000,000, 1 500,000 and 1 100,000 The report of biopsy of the right ear lobe was "inflammatory phase of lupus erythematosus"

The patient now presents an erythematous eruption involving both cheeks and most of the nose The shape of the eruption roughly resembles a butterfly There are telangiectatic vessels, and the scales are dry and adherent The lesions are sharply demarcated

Iodized salt was prescribed and the application of a sulfur preparation to the affected areas Within two weeks the eruption improved at least 75 per cent

DISCUSSION

DR PAUL E BECHET There is no doubt that the location is the usual one for lupus erythematosus and the scaling is characteristic, but the eruption lacks the follicular keratoses that one sees in the discoid type of lupus erythematosus This may be explained by the fact that the skin of young children is less apt to have keratotic lesions than the skin of adults I agree with the diagnosis The interesting thing is the age of the patient It seems to me that the incidence of lupus erythematosus in young children is greater today than it was years ago, and I believe that this is due to the increased tendency to exposure to the sun

DR RAY H RULISON I think that it is lupus erythematosus, probably of a superficial type

DR HOWARD FOX I agree with the diagnosis, particularly because histologic examination of one of the lesions confirmed it I do not agree with Dr Bechet that this disease is frequently seen in children It is most extraordinary to see 2 cases in babies at one meeting At least, it has never happened in my experience

DR GERALD F MACHACEK I do not know what else I would call this but lupus erythematosus Several years ago I saw 2 fairly well nourished children of this age group with lesions that were not as scaly as these but had the same distribution and also developed after exposure to sunlight The diagnosis was lupus erythematosus These children were on a diet of bananas, but appeared well nourished I do not know what ultimately happened, but I understand that they improved after the diet was varied The only clinical diagnosis I could make in the case presented by Dr Cipollaro would be lupus erythematosus, but I should consider the possibility that it might be due to or precipitated by some dietary imbalance, perhaps avitaminosis

DR A BENSON CANNON I agree with Dr Fox that lupus erythematosus in infants must be an exceedingly rare disease I do not recall having seen a typical

used and sensitivity of the Staphylococcus to penicillin has not been tested, I would advise that this be done

DR HOWARD FOX I am grateful for this discussion I shall see that the man has a roentgenogram of his lower teeth in a search for abscesses He has certainly had penicillin to the limit From what I have read, I have come to the conclusion that penicillin is often a poor remedy for sycosis vulgaris As to fractional doses of roentgen rays, I have had poor results I think that quinolor® ointment is the best remedy, though it may have to be continued for months As Dr Cannon said, it is not feasible in cases of profuse eruption to pull out all the hairs I shall advise the patient to rub in the quinolor® ointment vigorously three times a day

Lymphogranulomatosis Benigna (Schaumann's Disease) Presented by DR FRED WISE

A A, a Negro woman aged 35, registered at the Skin and Cancer Unit April 4, 1946, presenting lesions of four months' duration The patient had smallpox at 8, therapeutic abortion at 16 and supravaginal hysterectomy at 28 years She complains of weakness, cough, anorexia, constipation and nocturia During the past eight months she lost 33 pounds (15 Kg) in weight

On both parotid areas are symmetric hen's egg-sized fixed swellings Axillary and epitrochlear lymph nodes are enlarged The liver is enlarged to 3 finger-breadths below the costal margin The spleen is palpable and hypertrophied

Examination showed a pea-sized, raised, painless, nontender nodule on the upper lip and one on the chin, ten similar nodules are located on the small of the back and scattered isolated growths on the trunks and extremities Herpes zoster, in the form of a vesicular erythematous eruption, extends along the entire left sixth rib

The hemogram was normal Routine examination of the chemical content of the blood revealed 8 5 mg of urea nitrogen (normal 25 to 35), 21 mg of nonprotein nitrogen in one hundred cubic centimeters of whole blood (normal 160 to 230), 230 mg of cholesterol in one hundred cubic centimeters of plasma The icteric index was 7 1 The cephalin-cholesterol flocculation test gave a plus-minus result

Roentgenograms of the long bones showed small cystlike areas at the heads of several phalanges of both hands Examination of the eye revealed an enlargement of the peripheral portion of both lacrimal glands The orbital portion on the left side had a shotty feel On retracting the lower eyelid several match-head-sized nodules are exposed and hyaline-like excrescences at the upper borders of the tarsi of both lids are present There is no uveitis or iridocyclitis

The patient has chronic atrophic nasopharyngitis with suspicious small nodules on the uvula and a nodule on the laryngeal surface of the epiglottis and on the anterior commissure of the subglottis

The histologic section from one of the lesions showed Boeck's sarcoid Dr Charles F Sims interpreted the observations as follows The epidermis is somewhat flattened Throughout the upper middle part of the cutis and extending downward into the deep part of the corium are numerous well defined cellular masses composed of epithelioid and giant cells These masses do not appear to be undergoing necrosis There is little small round cell infiltration

baby was 3 months old, and since then it has spread persistently, without remissions, up to its present extent About four months ago lesions appeared on both forearms The child is decidedly undersized At the age of 15 months she weighed only 13 pounds (6 Kg) The baby was born without complications, and there were no unusual symptoms either before or after delivery

The patient presents an erythematous eruption involving both malar regions and extending across the bridge of the nose There are telangiectatic vessels and dry adherent scales, and the lesions are sharply demarcated There is one small lesion on the scalp and one small patch on each forearm A biopsy was not performed The patient was seen by me once, and then not again until the present time

Bismuth compound injections were advised, but the baby's pediatrician had read of the toxic effects of bismuth, causing death in 1 case, and he was therefore hesitant about using it Injections of crude liver extract were then recommended

DISCUSSION

Dr George C Andrews I agree with the clinical diagnosis, although I am not as positive as in the other case I should like to call attention again to the fact that the child's skin is delicate and different from that of the mother, who has a coarse skin That was true in my 2 cases

Dr Frank C Combes I agree with the diagnosis and think it represents a remarkable improvement

Dr Maurice J Costello I question the diagnosis This child must have some developmental defect which also affects the skin She does not appear to be a sick child I think that it is a cutaneous manifestation of a developmental defect, such as the telangiectatic type of streaking seen in some major ectodermal congenital defects

Dr J Gardner Hopkins I could not see much reason for calling it lupus erythematosus except for the involvement of the flush areas I saw no follicular plugging or hyperkeratoses There was a lesion in the elbow flexure which was eczematous, and I wondered whether it were not infantile eczema

Dr A Benson Cannon I agree with Dr Costello and Dr Hopkins that the eruption looks more like infantile eczema than lupus erythematosus The lesions are too diffuse, red, swollen and exudative for lupus erythematosus A further study of the case, including a biopsy, might help to make the diagnosis

Dr Gerald F Machacek I am less inclined to accept this as lupus erythematosus in view of the inanition and general underdevelopment My previous remarks are even more applicable to this case

Dr Howard Fox I agree that it is difficult to make a diagnosis in a child who is as restless as this one was The fact that the eruption began when the child was 3 months old makes it an exceedingly rare case of lupus erythematosus, if it is that disease The obvious developmental defect may have something to do with this eruption

Dr Ray H Rulison Aside from the distribution, I did not find much evidence to warrant a diagnosis of lupus erythematosus

Dr Eugene F Traub If we are to accept this as a case of lupus erythematosus, it would have to fit into the acute disseminated type, because the patient certainly does not present any of the characteristics of the discoid type As a matter of fact, Dr Hopkins and the others are probably correct in their feeling

DISCUSSION

DR GEORGE C ANDREWS I have as patients a brother and sister who have this disease limited to the palms and soles They have atrophy of the phalanges and the skin of the hands and feet The brother has some other lesions on his body but the sister has lesions only on her palms and soles My patients have atrophy and bullae, and atrophy of the digits, and present definite epidermolysis bullosa of fifteen years' duration This patient to my mind has hyperkeratosis and bullae I am not sure whether she has epidermolysis bullosa I presented a similar case before the New York Dermatological Society on Jan 23, 1945

DR J GARDNER HOPKINS This case reminds me of one reported in the November issue of THE ARCHIVES, also under the same diagnosis, with the disease limited to the palms and soles, but with no other signs of epidermolysis bullosa, and I wonder whether it was really that disease

DR HOWARD FOX I agree with Dr Hopkins I have received a number of articles from men in the Army or Navy describing cases with the condition limited mostly to the soles These men have eventually had to be discharged from the service They were often considered to be suffering from dermatophytosis at the outset, but eventually the correct diagnosis was made

DR MAURICE J COSTELLO This patient presents lesions almost at will After ironing clothes for a time large bullae develop on her palm, and always after walking three or four blocks bullae develop on her soles I have seen quarter-sized and half-dollar-sized, thick-walled bullae on her palms and soles

Widespread Papulosquamous Eruption, Neurosyphilis Presented by DR A BENSON CANNON

V V, a 42 year old Puerto Rican woman, was admitted to City Hospital for a generalized rash of three months' duration She had been in good health until three months prior to admission, when she suddenly began to experience severe frontal headaches, fever, malaise and anorexia At the same time there appeared a rash on the flexor surfaces of the arms and forearms The rash spread rapidly and became generalized The patient did not receive any therapy She was admitted to the hospital on April 15, 1946, having been referred from the Vanderbilt Clinic

The patient has been a widow for three years She has five children, all in good health The oldest is 25 years of age and the youngest 9 years One miscarriage occurred seven years ago

Physical examination discloses a well nourished Puerto Rican woman There is a generalized papulosquamous eruption involving the entire cutaneous surface, including the palms, feet and face Lesions are symmetric and superficial They are brownish red and covered with adherent scales The lesions resemble psoriasis The mucous membranes are not involved There are no lesions in the throat There are no lesions in the genital or anal regions The pupils react in accommodation but not to light The knee jerk is exaggerated, the ankle jerk is present The Romberg reaction is negative

The Ducrey and Frei reactions were negative Examination of the spinal fluid showed 12 cells, 0 01 per cent protein, colloidal gold 4444321000 Results of dark field examination of material from the lesions were negative on April 16 The Kline reaction of the blood was 4 plus on April 12 The Wassermann

whether this is a definite disease entity I think that we have seen enough cases now to justify its distinction from other dermatoses which it simulates I was interested to know that the man did not respond well to sulfapyridine We have had several patients who had good remissions definitely related to the administration of that drug

DR MAURICE J COSTELLO The only therapy I can think of which has not been tried is nonspecific therapy with triple typhoid vaccine injected intravenously I think that it would be beneficial, especially if combined with sunlight and salt water bathing, preferably in a southern climate

DR A BENSON CANNON The diagnosis of chronic discoid and lichenoid dermatosis had never occurred to me The patient is a wealthy business man with a happy disposition He has consulted me at infrequent intervals since 1933 for various minor dermatologic complaints Three years ago, I saw him for a few macular, pea-sized to five-cent-piece-sized, round to oval, scaly and crusted patches that were slightly itchy I diagnosed it as an eczematoid dermatitis due, probably, to a local irritant The lesions cleared with a few fractional doses of roentgen rays and tar ointment Since that time I have seen him every few months for a recurrence of the lesions, and there were never more than a couple of dozen After taking ocean baths in Florida and being in the sun, the patient noticed that all lesions disappeared, but these returned a few months after his return to New York Cultures for fungi were negative Patch tests elicited a strong reaction to pyrethrum, tar, phenol salicylate ointment, sulfur and several soaps Itching was never a pronounced symptom, and the lesions were always of the same character—macular, exudative, crusted areas There were never any nodules, plaques, pigmentation, lesions of the glans penis or adenopathy, symptoms that are usually found in chronic discoid and lichenoid dermatitis Tonight the patient presents many more lesions than I have observed before, but even now they are of the eczematous and crusting type

DR GERALD F MACHACEK I am of the opinion that many persons suffering from so-called chronic discoid and lichenoid dermatosis also suffer from an element of contact hypersensitivity and an element of cutaneous infection Recently in a biopsy in such a case I found a curious change in the coil glands, which appeared to be hypertrophic The inflammatory reaction seemed to reach well down into the secreting element of the gland

DR GEORGE C ANDREWS This man came to me in October, when he was worse than he is today At that time the lesions were widespread and oozing, and he was in a miserable condition He had been in Florida and knew the eruption would clear up if he went there again He said that the eruption came in cycles He is unmarried and worries a great deal He is in the textile business I have talked with his employer There is not much doubt in my mind that this is a case of chronic discoid and lichenoid dermatosis Dr Sulzberger examined him and agreed It interests me that he handles textiles, because I have another patient, a man who is a cotton goods salesman, and I know that Dr Sharlit had a patient sensitive to silk I have performed patch tests with cotton, rayon and silk, and all results were negative

DR EUGENE F TRAUB I should like the presenter to explain why these patients, particularly this one, appear to have been benefited by the warm climate Does he get anything by such a change except removal from his environment?

left cubital region On diascopic pressure there is no change in intensity of color

He is overweight His height is 5 feet and 5¾ inches (164 4 cm), and he weighs 172 pounds (78 2 Kg) stripped The abdomen is pendulous The breasts are prominent and the nipples retracted The genitals are small for his age Scrapings of the patches in the cubital region and axillas were negative for tinea on direct examination and culture

A histologic section taken from a hyperpigmented lesion on the neck according to Dr Charles F Sims showed the features of acanthosis nigricans for the most part, except for the absence of pigment He suggested that avitaminosis A be considered He stated that the epidermis was verrucous The granular layer was in part thickened and in part thinned, and at one or two points absent The epidermis was moderately and irregularly acanthotic with considerable interlacing of the rete pegs The basal margin did not present much pigment, as suggested by the clinical diagnosis There was a diffuse reaction in the papillary zone and a perivascular one in the subpapillary zone composed of small round cells, wandering connective tissue cells and scattered chromatophores Some interstitial and parenchymatous edema of the papillary zone were observed

DISCUSSION

Dr Henry E Michelson (by invitation) One reads in the literature of children with acanthosis nigricans occasionally experiencing something like the Cushing syndrome, but I think that the lesions of children with this disease will heal without any trouble

Dr Howard Fox The opinions that these lesions are benign are different from those expressed at the last meeting At that time, some members stated the opinion that some of these cases terminate fatally

Dr Hans J Schwartz The case that I reported some time ago was not of the juvenile type The patient was followed up at the Memorial and New York hospitals and died at the age of 53 years The case had been regarded as one of juvenile acanthosis nigricans, but autopsy showed an enlarged liver which proved to be carcinomatous

Dr William Curth (by invitation) I think that most of these cases of benign diseases continue without becoming cancerous In the cases of malignant disease there can be an interval of eight to ten years between the appearance of the cutaneous lesions and the manifestation of the cancer

Dr Fred Wise The consensus is that in these juvenile cases as a rule complications do not develop, but the patients have to be kept under observation until they reach maturity and adulthood

A Case for Diagnosis (Dermatitis Factitia of Both Feet) Presented by Dr Eugene F Traub

Rosacea-like Tuberculid of Lewandowsky Presented by Dr Fred Wise

Tuberculous Ulcerative and Fungoid Lesions of Buttocks and Perineum Presented by Dr Fred Wise

A Case for Diagnosis (Lichen Planus Pilaris? Parapsoriasis? Premycotic Stage of Mycosis Fungoides?) Presented by DR MAURICE J COSTELLO

Eosinophilic Granuloma of Pituitary Gland, Lungs, Bones of the Skull, and Skin Presented by DR GEORGE M LEWIS

M T, a woman aged 33, is presented from New York Hospital She was well until ten years ago, at which time she had severe polydipsia, polyuria, amenorrhea and loss of libido, clinically typical of diabetes insipidus Roentgen studies disclosed a normal sella turcica, but there were multiple rounded areas of destruction in the occipital and parietal bones, compatible with the diagnosis of eosinophilic granuloma of bone Similar lesions were demonstrated in the frontal region three years later At this time a necrotic area was found in the mandible, and on section it was found to be typical of eosinophilic granuloma of bone with "fairly dense connective tissue which was diffusely infiltrated by myelocytes of various forms and a great number of eosinophils" Four years after first observation, roentgen therapy, in a dosage of 400 r, was given to the osseous lesions of the skull and resulted in their complete involution There was no improvement in the diabetes insipidus following roentgen therapy, and symptoms, partially controlled by pitressin® (a preparation of the pressor principle of the posterior lobe of the hypophysis), have persisted to date

Granulomatous vulvar lesions were first noted four years after the onset of the disease These have gradually become more pronounced and extensive to date, six years later Eighteen months ago burning and redness were noted in the axillas and have been followed by the gradual development of granulomatous lesions similar to those on the vulva During the past four months low grade paronychial lesions and gradual destructive changes in the finger nails and toe nails have occurred

The axillas, vulvar region, perineum and adjacent aspects of the thighs are the seat of an extensive, moist, hypertrophic and vegetating granulomatous process The paronychial tissues are reddened and exude purulent material The nail substance has largely disappeared Chronic gingival lesions, now cleared, have resulted in the gradual loss of all the teeth

Repeated blood cell counts have revealed slight secondary anemia and inconstant, moderate leukocytosis Eosinophilia has never been detected Sternal marrow study was within normal limits Results of serologic tests of the blood were negative on several occasions Total protein was 8 Gm, the albumin-globulin ratio was 4 9 to 3 1, cholesterol values were normal Cultures from the granulomatous lesions have revealed hemolytic Staphylococcus aureus and Staphylococcus albus, nonhemolytic streptococci and a gram-negative bacillus resembling Bacillus Ducreyi Results of examination of curetted tissue for Donovan bodies were negative The reaction to the Frei test was negative Routine roentgen examination of the chest eight months ago showed a diffuse generalized eosinophilic infiltration in both lungs Results of examinations of the stool for ova and parasites have been negative on two occasions

A section taken from granulomatous lesions showed numerous large mononuclear cells, plasma cells and eosinophils, the latter occurring both perivascularly and diffusely through the section Moreover, eosinophilic granules were noted lying free in the tissue The blood vessels were the seat of extensive endarteritis

While the eosinophilic granulomas of bone disappeared after roentgen therapy, there has been no improvement in the diabetes insipidus to date The patient has

case of lupus erythematosus in a child under 3 years of age I think that it is necessary to observe such an eruption for some months and to have a biopsy made before one can be certain of the diagnosis of lupus erythematosus in infants Recently a baby was admitted to the hospital with the diagnosis of lupus erythematosus, but it proved to be infantile eczema In the case presented, the location and character of the lesions suggest the diagnosis of lupus erythematosus and the report of biopsy supports that diagnosis I should suggest, however, that the patient be observed longer and that another biopsy be made

DR JOHN C GRAHAM I think that it is lupus erythematosus, clinically at least I have never seen a similar case

DR MAURICE J COSTELLO I think that the patient has lupus erythematosus, and I think that it is the disseminated type, as there are lesions on the external surfaces of the forearms as well as on the face and neck It is the type of lupus erythematosus that will have to be watched carefully It would not be advisable to administer gold salts to this patient

DR FRANK C COMBES I agree with the diagnosis Of course, the youngster does look undernourished I agree with Dr Machacek, and there might also be an investigation as to tuberculosis in this family and in the child himself

DR GEORGE C ANDREWS The delicate character of this child's skin should be noted About two summers ago I saw 2 children, about 2 or 3 years of age, with lupus erythematosus One was in New York Hospital for a month under observation, and the diagnosis was well established These patients have both improved I have seen them within the past six months The improvement was great with proper diets, with a great deal of vitamins, wheat germ and injections of crude liver extract Both have slight traces of disease but are greatly improved They had the extensive discoid type of lesions on the face

DR NIELS DANBOLT, Oslo, Norway (by invitation) I agree with the diagnosis It is surprising to see lupus erythematosus in such small children I am of the opinion that you see more of this disease here than we do in Norway I can not understand why you use the name "lupus" In Scandinavia we have dropped that misleading term altogether and call it just "erythematodes"

DR GEORGE M LEWIS From the clinical features presented, I would favor lupus erythematosus over other diseases with which the disease could be confused

DR EUGENE F TRAUB My co-workers and I saw this patient at the New York Skin and Cancer Unit several months ago, within a short time following his summer exposure to sun He presented a classic type of discoid lupus erythematosus, and the features that were present then, namely, the dilated follicular plugs and what appeared to be superficial atrophy, are not so apparent now A biopsy was performed to confirm the diagnosis chiefly because of age of the patient

DR ANTHONY C CIPOLLARO I also thought that lupus erythematosus was extremely rare in children of 3 and under, and for that reason I am presenting 2 cases I think that the diagnosis has been well established in this case, both clinically and histologically, and I should also like to emphasize the improvement which followed treatment with iodized salt

Lupus Erythematosus Presented by DR ANTHONY C CIPOLLARO

M Z, a girl aged 19 months, born in the United States, was first seen by me on July 25, 1946 The mother first noticed a rash on the right cheek when the

I have had at least half a dozen patients in my practice for whom the diagnosis of malignant melanoma was made and confirmed by histologic study who have done well One has survived six years, a second nine years and a third ten years

DR GEORGE C ANDREWS I have seen superficial lesions of this character which continue for a long time However, I believe that the histologic diagnosis would be melanoma

DR. GEORGE M LEWIS If melanoma is seriously considered here, transillumination is a valuable method to demonstrate the extent of the lesion It is my impression that the lesion is a pigmented basal cell epithelioma or possibly a pigmented nevus and not a melanoma

DR PAUL E BECHET I greatly appreciate the discussion because of the involved therapeutic problem The fact that the lesion has been continuously present for thirteen years, with increase in size only in the past year, does in my opinion prove the presence of a low grade or transitional type of malignant process The patient denies the existence of any lesion on her cheek prior to the present one, so that it apparently occurred d'emblée sixteen years ago The opinions expressed in the discussion are somewhat divided as to whether or not one should intervene I shall take them carefully under consideration before making a decision, but my impression is that we are dealing with a malignant lesion which, though present for sixteen years with no apparent metastasis or much increase in size, remains potentially dangerous and that it would be better to excise it widely and subject the tissue to microscopic examination than to leave it severely alone, with possible fatal results in the future

Necrobiosis Lipoidica (Without Diabetes) Presented by DR GEORGE M LEWIS

Leukoplakia of Buccal Mucosa (Excellent Result from Treatment with Electrodesiccation) Presented by DR A BENSON CANNON

Tuberculoid Leprosy. Presented by DR. MAURICE J COSTELLO

E P, a boy aged 5, from Willard Parker Hospital, was born in Puerto Rico His father died of pulmonary disease, and his mother is in a leprosarium in Puerto Rico She has had the disease at least seven years The boy was brought to New York by plane via Miami on June 23, 1946 He had about a dozen somewhat hyperpigmented, sharply circumscribed, dime to quarter-sized lesions with a thin, raised border These lesions are anesthetic to cold, heat, touch and the prick of a pin The ulnar nerves are enlarged, and the greater auricular nerve can be palpated

The Wassermann reaction of the blood was negative, as were the reactions to the Kline diagnostic and Kline exclusion tests Nasal scrapings were sterile Biopsy of one of the lesions showed the corium in the center of the section to be granulomatous, consisting of pale mononuclear cells, some with foamy cytoplasm, and a small number of lymphocytes Occasional fibroblasts were present in the periphery of the lesion The character of the granuloma was identical with the leprous lesions from our material at the hospital, but no acid-fast bacilli were found in the section with Fite stain (Dr Vero Dolgopol)

that this patient may not have lupus erythematosus at all, but that the hyperactivity of this child may be responsible for some of her cutaneous lesions It appears that the child rubs the face and in this manner brings about some, if not all, of the erythema and irritation The lesion on the flexor surface of the forearm is definitely edematous and vesicular and suggests either a patch of eczema or possibly even an artefact My suggestion would be for Dr Cipollaro to hospitalize the child and restrict the motions in such a way that she cannot rub her face or roll the head on the pillow and observe whether this does not cause an amelioration of the symptoms

DR ANTHONY C CIPOLLARO My diagnosis is based on two hasty observations When I saw the child the first time, I thought of several diagnoses, such as developmental defect, psoriasis, eczema and lupus erythematosus In favor of lupus erythematosus are the persistence, steady spreading, demarcation, dry adherent scales, absence of remissions and lack of vesiculation The child's pediatrician has never thought of eczema in this case The diet has been carefully supervised There is no history of atopy in the family. It is true that I did not find keratotic plugs, but in a child with a delicate skin one does not expect to find the same degree of scaliness or follicular plugging as in an adult Against eczema is the lack of vesiculation and crust formation As far as developmental defects are concerned, I could not see any evidences of nevus flammeus, and it is not like any other developmental defect I know I think that the fact that the mother is small has a good deal to do with the child's small size The evidence as I see it favors a diagnosis of lupus erythematosus I shall discuss the question of performing a biopsy with the pediatrician, and if he and the mother consent, I shall proceed with biopsy

Chronic Discoid and Lichenoid Dermatosis Presented by DR GEORGE C ANDREWS

J G, a Jewish man aged 50, was first seen Oct 9, 1946, with an eruption which had had its onset fifteen years previously, beginning with a small lesion on his thigh This had spread gradually The dermatitis had cleared with roentgen therapy, ultraviolet irradiation and various injections Exacerbations occurred at intervals but responded with the described treatment The patient has noticed also that healing occurred spontaneously during vacations in Florida There was a history of eczema during infancy Allergy testing in 1931 revealed a positive reaction only to orris root

Examination shows a patchy, vesicular, papular, erythematous discoid and lichenoid dermatitis on the body and particularly on the extremities and penis

A complete blood cell count revealed 96 per cent hemoglobin, 4,720,000 red blood cells and 5,850 leukocytes The differential smear showed 16 per cent eosinophils The urine was normal

The patient has shown no improvement with the parenteral use of penicillin, oral use of sulfapyridine, an elimination diet or arsenic trioxide solution given intramuscularly Local treatment has consisted of mild antipruritic applications and superficial roentgen therapy

DISCUSSION

DR FRANK C COMBES This man presents practically all of the characteristics one usually associates with this disease In all cases the question comes up as to

DR GERALD F MACHACEK It is my impression that a number of the patients that Dr Cannon sent to Texas were persons who handled textiles, and particularly tailors who handled dirty garments

DR GEORGE C ANDREWS My other patient was in Presbyterian Hospital for several months and was seen in consultation by Dr MacKee, who agreed with the diagnosis of chronic discoid and lichenoid dermatosis The eruption cleared up temporarily after electric shock treatments He stayed well for about three weeks and then started worrying, and the eruption recurred He went to a doctor in New Jersey who continued shock treatments and telephoned me that the man was completely cured I said that I would like to hear from him again in about six months Later he told me that the patient was again ill There is certainly a large psychic element in this disease

Knuckle Pads Presented by DR J GARDENR HOPKINS

E M, a married woman aged 40, presents thickening of the skin over the proximal interphalangeal joints of all fingers, but not of the thumbs or toes These have gradually developed over a period of eighteen months There have been no subjective sensations The patient works as a secretary and office nurse There is no history of injury or of rheumatic fever

The lesions form disks 10 to 15 mm in diameter These are firm, inelastic and apparently formed by thickening in the cutis or subcutis without notable epidermal change

Roentgen examination showed no changes in the bones Biopsy showed dense collagen with some evidence of degeneration but no characteristics on which to base a diagnosis

DISCUSSION

DR FRANK C COMBES The only treatment I know of is protective—the lesions should be covered with elastoplast for several months Knuckle pads do not respond well to irradiation

DR MAURICE J COSTELLO This woman has knuckle pads on the second, third and fourth fingers, but none on the thumb I think that if her household activities were carefully studied one could find the cause

DR HOWARD FOX I agree with the diagnosis, but I do not know of any treatment that cures the disease We talk the problem over perennially and get nowhere, except that we agree that none of us has ever seen a case in which it could be proved that trauma was causative

DR RAY H RULISON Some patients have Dupuytren's contracture, which is apparently not a part of the picture and yet it does occur later in some cases

DR GEORGE M LEWIS In a patient with a rather typical lesion temporary improvement was obtained by the use of moleskin adhesive plaster, continuously applied, as first advocated by Kest Moleskin seems more effective than ordinary adhesive plaster

A Case for Diagnosis (Pemphigus Vulgaris? Dermatitis Factitia?) Presented by DR GEORGE C ANDREWS

A Case for Diagnosis (Dermatophytosis? Pustular Psoriasis? Bacterid?) Presented by DR EUGENE F TRAUB

Monilia Results of roentgen examination of the chest, gallbladder and gastrointestinal tract were essentially normal except for a suggestion of periduodenitis and colonic hypermotility with general irritability and spasm The result of cystoscopic examination was negative for infection or tumor The results of Pels' tests on three occasions were positive

Ophthalmologic examination has shown chronic blepharokeratoconjunctivitis of unknown cause, which has recurred about every three months Topical application of penicillin has produced only temporary improvement

Blood cell counts have shown leukocytosis, with the count varying from 8,200 in 1933 to 23,500 in September 1946, with lymphocytes varying from 35 to 82 per cent

Treatment has included vitamins, acetarsone, and sulfonamide drugs given orally, with parenteral administration of neoarsphenamine, oxophenarsine hydrochloride, bismuth compound, liver, eschatin® (an extract of the adrenal cortex), moccasin venom, autogenous mixed vaccine, penicillin and typhoid vaccine and autohemotherapy His condition is essentially unchanged

DISCUSSION

DR HOWARD FOX I think that Dr Traub's suggestion of Behcet's syndrome is correct The eruption involves the three favorite areas of this disease, namely, the mouth, eyes and genitalia The disease has been extremely chronic, as it always is, and treatment has been of no permanent benefit Dr Traub has been persistent for seventeen years in trying various methods of treatment, without success

DR A BENSON CANNON This is one of the most interesting cases I have seen for a long while, and I cannot offer any better suggestion than has already been brought forward I would classify the case as one of lymphoblastoma I believe that the location of the lesions is common in leukemia, and their infiltration, the deep, verrucous ulceration on the palate and the blood cell counts would cause me to think of leukemia rather than any other form of lymphoblastoma I should suggest that another biopsy be made of the skin and one of the ulcer on the palate and that the blood and bone marrow be studied by a hematologist The slowly progressive nature of the disease, the increased total white blood cell count and lymphocyte count indicate a bad prognosis Leukemic states can last for years

DR GERALD F MACHACEK My conception of Behcet's disease is that it is a condition which recurs and is essentially vesicular The infiltration on the face makes me agree with Dr Cannon that leukemia is certainly one of the differential diagnoses that must be considered I would also suggest that the presenter check the history again to ascertain whether the patient is not taking phenolphthalein in some occult form

DR J GARDNER HOPKINS I believe that the lesions of Behcet's syndrome are ulcerations resembling aphthae This man's lesions on the penis have never ulcerated The ulcerations described by Behcet do not extend in a serpiginous manner as the lesion on the palate has done in this case Dr Cannon's suggestion that this is leukemia seems more plausible, though it is a little difficult to reconcile with the history that thirteen years ago he had a chronic ulceration on the cheek without blood changes

DR. GEORGE C ANDREWS I do not think that it is Behcet's syndrome Iritis and hypopion are not present The lesions in Behcet's syndrome, as Dr Hopkins

gained 25 pounds (11 Kg) in the past ten years The cutaneous lesions have shown gradual improvement following various types of local therapy and the administration of roentgen rays

DISCUSSION

DR GERALD F MACHACEK I do not wish to take issue with the diagnosis, but there are indications here of what might be called multiple myeloma From a section of the skin, and taking into consideration that the blood cell count was within normal limits, I think that the changes suggest aleukemic leukemia, from the many monocytic cells within the vascular lumens

DR MAURICE J COSTELLO I think that Dr Lewis, about three years ago, presented a case of eosinophilic granuloma confined entirely to the skin, with a large tumor mass on the back

DR GEORGE M LEWIS This case is almost unique in that there is authenticated involvement of bones, lungs and skin It is interesting that roentgen therapy is rapidly successful in curing the bone disease and apparently in curing the lung disease Roentgen therapy has also helped the cutaneous lesions in this patient The essential histologic changes appear in the blood vessels, which at first show swollen endothelial cells with progressive endarteritis with narrowing of the lumen The infiltrate at first is focal but later diffuse through the tissues The infiltrate also changes from a polymorphous type to one predominantly eosinophilic

Solid Edema of the Face and Neck Occurring in the Course of Infectious Eczematoid Dermatitis Presented by DR MAURICE J COSTELLO

Eugene F Traub, M D, *President*
George M Lewis, M D, *Secretary*
Jan 28, 1947

A Case for Diagnosis (Melanoma?) Presented by DR PAUL E BECHET

V P, a woman aged 53, stated that sixteen years ago she noticed a small tumor on her right cheek which increased considerably in size within a year It was removed but in what manner she does not remember Two years later it recurred, and in the past thirteen years no attempt has been made to treat it In the past year the patient states that the lesion has increased in extent On inspection, she presents a dark red patch about 50 mm in diameter, with a distinct, elevated and indurated border and in its upper part a black, sharply outlined, somewhat raised, rounded area about 30 mm in diameter The patient states that the melanotic features have been present for six years Her health is good, and there is no evidence of metastasis anywhere There are no similar lesions elsewhere on her body

DISCUSSION

DR JOHN C GRAHAM I would have a plastic surgeon remove the lesion, which is commencing to show malignant changes It is undoubtedly melanotic, and I think it should be widely removed and a graft set in

DR MAURICE J COSTELLO As the lesion has been present for sixteen years, I would be inclined to do nothing radical It may last another sixteen years

vaccination "take" developed, surrounded by a palm-sized area of erythema and edema The following day two marble-sized, thick-walled, tense bullae appeared on either side of the vaccination These are diagnosed as bullae of epidermolysis bullosa occurring on a site of edema and erythema and probably caused by trauma, such as scratching They were not secondary vaccination inoculations The patient has epidermolysis bullosa of the acquired type for which she has been treated for some months in the clinic Typical lesions of the disease were found on the nails, elbows, knees and other points of trauma

DISCUSSION

DR HOWARD FOX The patient shows signs of epidermolysis bullosa of the nails It does not seem like a spread of the vaccination or autoinoculation The lesions are in a region which has been more or less traumatized, and one should accept the possibility that these bullae are part of her old disease

DR PAUL E BECHET I agree with the diagnosis The trauma involved in the performance of a vaccination is enough to cause an extension of lesions of epidermolysis bullosa, which is precipitated in any location by trauma

DR RAY H RULISON I agree with the diagnosis, and I agree with Dr Combes that the trauma arises not from the superficial scarification but from the virus I can readily see how irritation and infiltration would precipitate lesions in a patient with this disease, but I have seen almost as severe reactions in persons without this disorder

DR JOHN C GRAHAM I do not quite agree with Dr Combes that scratching could not cause the lesions If her vaccination itches as mine does, she could get the blebs of epidermolysis bullosa from scratching I think that she has traumatized it

DR EUGENE F TRAUB This could well be an example of a dystrophic type of epidermolysis, and in that type particularly blisters will appear spontaneously and with the least provocation I feel that this insult was more than adequate to cause such a change and agree that vaccination was responsible

Neurofibromatosis, Ichthyosis Presented by DR GEORGE M LEWIS

Dermatitis Medicamentosa (Demerol®), Addisonian Pigmentation (Arsenical Keratosis and Pigmentation?) Presented by DR GEORGE M LEWIS

A A, a man aged 45, a former taxicab driver, had minimal pulmonary tuberculosis five years ago Two years ago a diagnosis of Addison's disease was made at the New York Hospital, and this has been treated with 6 Gm of salt and 4 Gm of desoxycorticosterone acetate daily One year ago keratotic lesions on the palms and soles were first noted Two months ago the patient had severe neuritic pains in the legs, for which he has been taking 50 mg of meperidine hydrochloride (demerol®) daily About three weeks ago a pruritic, burning, erythematous, diffuse eruption developed on the extremities and later on the trunk, and this eruption soon became dry and scaling There is no obtainable history of arsenic ingestion

A diffuse, erythematous, dry, scaling eruption over the extremities and trunk is present There are keratotic lesions on the palms and soles, and keratotic

Dr Jackson claimed that she isolated gram-positive, non-acid-fast forms from the cutaneous lesions It is interesting to note that this patient, though exposed to acute contagious diseases while at the hospital, did not become infected with any of them

DISCUSSION

Dr Gerald F Machacek I saw the child several months ago and suggested treatment with streptomycin with hesitation, as this is a "benign" form of leprosy

Dr Fredrick Reiss (by invitation) I believe this case is one of typical minor tuberculoid leprosy

Dr A Benson Cannon I suggest that the patient be treated with diasone® by mouth, beginning with small doses and gradually increasing the dosage Dr Faget reports excellent results in the treatment of leprosy with that drug and states that it is less toxic than other preparations He states that the patient must take the medicine for six months or longer before improvement can be noticed

Dr Maurice J Costello I have tried streptomycin in cases of this disease, without the slightest benefit

Granuloma Inguinale of the Mouth and Genitalia Presented by Dr A Benson Cannon

E S, a Puerto Rican woman aged 26 who has been in the United States for six years, was admitted to the City Hospital on Jan 9, 1947, complaining of sores in the mucous membranes of the mouth, lips and anal-genital region of twelve months' duration The patient has been separated from her husband for five years She has never been pregnant. The past and family histories are essentially noncontributory

The present disease began with a small ulcer near the anus twelve months ago, which gradually increased in size, spreading around the anus and the crotch to the front and involving the inguinal regions and the vulva with an extensive ulceration which is painful on motion

Note.—Donovan bodies were subsequently found in the oral lesions and also in the genitocrural ulcer The patient was given three small blood transfusions of 250 cc each and an injection of fuadin® every day The improvement has been spectacular There was immediate relief from pain, so that the patient eats well, can walk and has gained 20 pounds (9 1 kg) in weight On February 24 most of the oral lesions were gone and those in the groin were noticeably better Of the last 65 patients with granuloma inguinale admitted to hospitals, this is the second to have lesions of the oral cavity

Fox-Fordyce Disease Alopecia Areata Presented by Dr George C Andrews

R M W, a Negro woman aged 20, single, is presented from the Vanderbilt Clinic She was first seen in October 1946, with a pruritic eruption of one year's duration, which had appeared after taking injections from her private physician to "stimulate hair growth" Episodes of partial loss of hair had recurred over a period of ten years The eruption began in the axillas and had spread to involve other areas There has been no exacerbation at the time of the menses, which have been regular until the past month, when a mild metrorrhagia occurred

Pustular Psoriasis Presented by DR GEORGE M LEWIS

H J, a white woman aged 36, has had a recurrent pruritic vesiculopustular eruption on the soles for the past five years The pruritus is worse during the menses She was treated for three years with benzoic and salicylic acid (Whitfield's) ointment, aluminum acetate (Burow's) solution and ointment, boric acid and salicylic acid powders, naphthalan, ichthammol, crude coal tar, ammoniated mercury, sulfur, brilliant green, tannic acid, boric acid ointment and roentgenotherapy, with little if any improvement

When I first saw her, two years ago, penicillin ointment was used without success Thereafter for six months she was given intravenous injections of 1 per cent antimony potassium tartrate, supplemented with four fractional doses of roentgen rays and quinolor® ointment (a mixture of three chlorine derivatives of 8-hydroxyquinoline in a base of equal parts of petrolatum and wool fat) This therapy resulted in almost complete involution of the eruption The patient then used chrysarobin ointment and stannoxyl® (a combination of metallic tin and its oxide) tablets There was considerable improvement for several months, with only a few transient vesiculopustules and mild pruritus One year ago another exacerbation occurred Pyorrhea was treated at this time Results of roentgen examination of the teeth were normal The eruption gradually subsided, and the patient was free of lesions until three months ago, when the present relapse began A course of sulfadiazine, 4 Gm daily for two weeks, was given and an ointment containing resorcinol, salicylic acid and chrysarobin was prescribed

An extensive vesiculopustular eruption is present on the palms and soles The lesions are grouped in patches on the soles The nasal and oral cavities are normal, and there are no other evident foci of infection The result of urinalysis was normal, the Wassermann reaction of the blood was negative and cultures were negative for fungi

DISCUSSION

DR EUGENE F TRAUB I have tried antimony potassium tartrate, with the same results Dr Lewis reports temporary slight improvement followed by a return of the eruption I do not believe that it is possible to determine whether the tonsils are actually a focus in a given case even if pus is aspirated from them While it is certainly better to determine in advance that there is an infection in the tonsils, removing infected tonsils does not necessarily cure the eruption In 1 instance in which this was the case I discovered that the patient had an infection in his prostate which was thought to be secondary to the tonsillar infection Improvement followed prostatic massage

DR GEORGE M MACKEE According to histologic work that has been done recently, these conditions can be divided into two varieties One is psoriasis histologically, and the other is not Differentiation may make a therapeutic difference What was said about antimony potassium tartrate therapy is true about every possible treatment for this disease Everything tried has been successful only temporarily, except perhaps removal of foci of infection In spite of the fact that there is no cure, the majority of patients eventually recover

DR HOWARD FOX I agree with the presenter that it is proper to tell the patient, as Dr Andrews does, that it is not certain that he will get well after tonsillectomy, regardless of what organism is found on aspiration I should certainly suggest that this patient have her tonsils removed

Psoriasis and Pustular Psoriasis Presented by Dr George M Lewis

A Case for Diagnosis (Hypostatic Eczema? Purpura? Kaposi's Sarcoma?) Presented by Dr Maurice J Costello

Tinea Capitis in a 16 Year Old Girl (Previously Presented at the Manhattan Dermatologic Society Oct 8, 1946) Presented by Dr Anthony C Cipollaro

Scleroderma, Generalized Presented by Dr Eugene F Traub

Psoriasis Toxic Eruption Secondary to Dermatophytosis Blue Nevus Presented by Dr Eugene F Traub

Kaposi's Sarcoma Resembling Granuloma Pyogenicum Presented by Dr Anthony C Cipollaro

Tertiary Syphilis Presented by Dr Maurice J Costello

Eugene F Traub, M D, *President*

George M Lewis, M D, *Secretary*

Feb 25, 1947

Ulcer (Postdesiccative, Left Thumb) Xeroderma Acarophobia Neurotic Excoriations Presented by Dr George M Lewis

A Case for Diagnosis (Behcet's Syndrome? Pemphigus? Leukemia Cutis?) Presented by Dr Eugene F Traub

I M, a man aged 52, has been previously presented He was first seen at the Skin Clinic of the New York Post-Graduate Hospital in 1930 when on otolaryngologic examination bullous lesions were discovered on his palate About the same time the patient noticed a sensation of stiffness of the upper lip He then reported to my office, where he has since been a private patient

On Aug 7, 1931, the patient presented an ulcerative lesion on the roof of the mouth, of long duration, which finally healed after wide endotherm removal In 1932, erythematous, scaly lesions appeared on the upper lip and in both nasolabial folds Tonsillectomy was performed Apart from the period 1932-1934, during which time the patient was entirely free of lesions, there was a continuous appearance of lesions in the mouth and buccal mucosa, as well as on the mucosa of the hard and soft palate, together with erythematous, scaly, psoriasiform lesions on the lips, nasolabial folds, eyebrows and penis

On the buccal mucosa at present there are several rounded, denuded areas about 1 to 1 5 cm in diameter The uvula is thickened and shows small ulcerations There are ill defined, confluent, polycyclically outlined ulcerations on the eyebrows, lips and glans penis, with flat, necrotic, scaling, moderately infiltrated, erythematous lesions The region around the chin is diffusely involved by a brown-red, scaly, infiltrated erythema

Results of urinalysis and Wassermann tests of the blood on many occasions have been negative, as were smears for Vincent's organisms and cultures for

remissions and exacerbations over a period of several years, and the condition is resistant to therapy

DR EUGENE F TRAUB Does the patient take aminopyrine?

DR ANTHONY C CIPOLLARO She does not take any medicine A culture for Monilia was made at the Lahey clinic, and it was negative I considered pemphigus, as did some of the men at the Lahey Clinic, but thus far she has had no more manifestations than she showed tonight I shall have to observe her further

Multiple Vaccination of the Face (from Barber Shop?) Presented by DR EUGENE F TRAUB

G R, a man aged 68, was first seen May 7, 1947, complaining of an eruption of eight days' duration He had not been vaccinated but had been shaved by a barber twice weekly prior to the appearance of the eruption It was not determined whether the barber had been vaccinated or whether he had had recent contacts which might have resulted in the vaccination of the patient An adult son had been vaccinated but lived separately from the father, and little or no contact had occurred between them preceding the infection The probability is strong that the vaccination occurred in the barber shop

The patient's appearance was striking, as all lesions were located in the bearded area There were at least thirteen lesions, but several on the right side of the chin had become confluent, so that there was now one huge, inflamed and necrotic mass Most of the other lesions had remained discrete and were present on the left side of the chin and on both cheeks All had the appearance of strong vaccination "takes," and consisted of inflamed bases with pustular and necrotic centers Some were slightly crusted Healing was uneventful, and most of the lesions, including even the large confluent one, had disappeared completely in ten to fourteen days Deep scarring marks the site of the confluent area, but the remaining lesions have left only superficial redness, which may disappear entirely

DISCUSSION

DR HOWARD FOX I think that it is possible that the patient acquired the vaccinia in the barber shop A number of years ago I was lecturing at New York University on eczema and mentioned that one of the dangerous sequelae was vaccinia, saying that no child with eczema should be vaccinated While lecturing I got a note from the pediatric department asking me to come to Bellevue Hospital to see a child The child was a 2 year old Negro with typical lesions of vaccinia on a large part of the body, which he had contracted from an older sister who had recently been vaccinated He died in about six days

DR ANTHONY C CIPOLLARO The thought came to me that these sequelae might be prevented by covering vaccinations Patients rub and scratch and reinoculate, and for this reason I have covered vaccinations in members of my family and in my own case I think that it prevents this sort of accidental vaccinia

DR EUGENE F TRAUB I thought that I had fairly well excluded all sources of inoculation but the barber shop The only other member of the family who had been vaccinated was an adult son, who did not use the same bathroom as his father

Sarcoidosis in a Negro Woman Aged 33 Years Presented by DR. A BENSON CANNON

DISCUSSION

DR EUGENE F TRAUB Clinically this is not a case of pseudoxanthoma elasticum, because, in addition to being more yellowish, this disease tends to run in transverse striations along the neck and the lesions, while slightly elevated, appear to be atrophic I do not believe that the patient has poikiloderma of Civatte The characteristic telangiectatic vessels, recticulated network, small papules and peculiar pigmentation accompanying that disease are lacking here I agree that this patient has some changes which suggest either scleroderma or dermatomyositis, and there are some deep-seated, thickened rather than atrophic lesions present The patient should be studied further

Psoriasis, Granuloma Annulare, Urticaria Presented by DR ANTHONY C CIPOLLARO

Atopic Eczema, Congenital Abnormalities, Vascular Nevus, Elephantiasis, Undescended Testes Presented by DR EUGENE F TRAUB

Chronic Lupus Erythematosus (with Associated [?] Deafness) Presented by DR GEORGE M LEWIS

Infected Preauricular Branchial Cysts Presented by DR MAURICE J COSTELLO

T B, a boy aged 15, has in the preauricular regions two nearly dime-sized, slightly elevated, red, somewhat infiltrated lesions In the center of each is a tiny hole from which pus exudes on slight pressure Above and posterior to these are two oval indentations measuring about 3 mm, located at the root of the helix The latter are seen from time to time in persons with or without other congenital anomalies They are often familial They are the upper openings of the partially obliterated branchial clefts The explanation of the sinus openings is that the purulent material in these cysts drains by gravity through the skin in these locations The patient has been referred to an otolaryngologist for excision of the cysts

DISCUSSION

DR HOWARD FOX I agree with the diagnosis This infection did not go through the normal channel, and it caused an impetiginous patch where it broke through the skin

DR GERALD F MACHACEK Cancers are known to arise in branchial clefts Oncologists place special emphasis on this observation

DR EUGENE F TRAUB Injections of iodized poppyseed oil might cause trouble The tract may go much further or branch off in a different direction than is taken by the oil, so that a false impression might be obtained In addition, there are other complications from this process that render it inadvisable

DR GERALD F MACHACEK I have seen iodized poppyseed oil forced into tissue with the resultant formation of granulomas which look like sarcoids but are really similar to paraffinomas

Bullae of Epidermolysis Bullosa Occurring on a Vaccination Site Presented by DR MAURICE J COSTELLO

Mrs S B, aged 70, from the Bellevue Hospital outpatient department, was vaccinated in the left deltoid region April 14, 1947 A week later a dime-sized

Biopsy at Harlem Hospital showed cutaneous nodular leprosy

Roentgen examinations at Willard Parker Hospital showed destruction of the tufted ends of all terminal phalanges of the fingers and toes There was periostitis of the proximal phalanges of all four fingers of the right hand

Results of roentgenographic examination of the chest were normal, ruling out sarcoid The Kline reaction of the blood was 4 plus, and the Mazzini reaction was negative Determinations of the chemical content of the blood showed a reversal of the albumin-globulin ratio, the albumin being 2 Gm and the globulin 6 Gm A blood cell count revealed 4,260,000 red blood cells and 11,500 white blood cells, with 65 per cent polymorphonuclear leukocytes, 24 per cent lymphocytes, 7 per cent eosinophils and 3 per cent large mononuclear cells The urine was repeatedly normal A nasal smear showed lepra bacilli

DISCUSSION

DR HOWARD FOX The man who made the original diagnosis, probably Dr Irgang at Harlem Hospital, is entitled to much credit The patient comes from a country where leprosy is endemic, but one must examine him carefully to discover any changes The ulnar nerves are unquestionably enlarged all the way to the axillas, and one may press on them hard without causing any pain, which is much in favor of leprosy There are nodules on the ear and some enlargement of the great auricular nerve, although there is no anesthesia In a recent article Arnold expressed the belief that examination of the nasal smear for lepra bacilli is of little diagnostic help It is not the best way to prove a diagnosis of leprosy The radiologic changes in the phalanges in this case are significant

George M Lewis, M D, *President*

John C Graham, M D, *Secretary*

Nov 25, 1947

Lichen Planus Limited to the Oral Mucosa Presented by DR GEORGE M LEWIS

E S, an American lawyer aged 43, discovered an asymptomatic white lesion on his tongue eleven months ago Six months later he saw his physician and then an oncologist, both of whom made a diagnosis of leukoplakia

The patient smoked two pipes and fifteen cigarets daily, used magnesia magma as a mouthwash and a magnesia magma tooth paste He took a "vitamin pill" daily and a "sleeping pill" every two weeks In June 1947, when I first saw him, there was a bluish white lesion on the dorsum of the tongue about 2 by 1 cm in extent, an area similar in appearance was present inside the cheek opposite the lower right molars A circinate lesion was found near the oral commissure on the buccal mucosa of the left cheek

The patient has not smoked since June He is using a bland mouthwash Partial involution of the lingual lesion has occurred, but those on the buccal mucosa have remained unchanged

DISCUSSION

DR HOWARD FOX It is sometimes difficult to differentiate between leukoplakia and lichen planus, but as Dr Combes said, leukoplakia tends to be thickened and rough and even verrucous, which lichen planus does not Without biopsy, it is difficult to tell in some cases I think that this patient probably has lichen planus

lesions arise from the skin of the body, especially on the shoulders Many pigmented brown macules are present, especially on the back and shoulders

A complete blood cell count showed 4,400,000 red blood cells, 3,800 white blood cells and 13 Gm hemoglobin, with 59 lymphocytes, 7 monocytes, 14 eosinophils, 20 polymorphonuclear leukocytes (mature forms 16 and band forms 4) Blood sodium was 325, potassium 16 25, and cholesterol 185 mg Results of biopsies have not been reported

DISCUSSION

DR HOWARD FOX This man has a striking and profuse pigmentary eruption As the pigment is in the form of small macules and not a diffuse pigmentation, it is certainly not typical of Addison's disease and looks more like arsenical pigmentation Arsenic, however, does not produce pigment in the mouth, whereas Addison's disease does, and there is one small pigmentary patch opposite one of the patient's molars I still think that the whole picture is probably one of arsenical pigmentation

DR PAUL E BECHET There is no dermatologic condition I know of that presents this picture of lentiginous pigmentation, particularly on the shoulder blades The few patients with Addison's disease I have seen show more diffuse pigment, with generalized bronzing The patient does not have the dry skin and furfuraceous scaling so common in arsenical dermatoses

DR RAY H RULISON If this case had been presented as one of arsenical pigmentation and keratosis, with no history of Addison's disease, I think that one would accept it without question However, this case has been carefully studied, and, as I understand it, the patient has never been given arsenic and no excessive arsenic has so far been found If this man has Addison's disease I do not believe that it is fair to say that he must have arsenic retention and that the pigmentary changes are due to that, because they conceivably could be Arsenic should not be part of the diagnosis until it has been demonstrated

DR JOHN C GRAHAM Could the amount of treatment he has had affect his pigment?

DR GERALD F MACHACEK Pigmentary changes in Addison's disease need not be characteristic I saw photographs of patients with Addison's disease that curiously showed leukoderma Dr Potelunas tells me that the patient was admitted to the hospital in a crisis at one time

Eugene F Traub, M D, *President*

George M Lewis, M D, *Secretary*

May 27, 1947

Cavernous Hemangioma (Angioma Venosum Racemosum) Presented by DR MAURICE J COSTELLO

Hairy Nevus of the Scalp Presented by DR FRED WISE

A Case for Diagnosis (Parapsoriasis? Iododerma?) Presented by DR PAUL E BECHET

unchanged up to the present On elevation of the feet, the edema shifts to the thighs and abdomen Hematologic studies at Mount Sinai Hospital showed essentially normal conditions except for hypoproteinemia The report of protein fractionation revealed reduction of all protein fractions, with complete absence of gamma globulin

Studies at Bellevue Hospital showed a total protein content of 5 2 Gm with albumin 2 6 Gm and globulin 2 6 Gm The cephalin-cholesterol flocculation reaction was negative On another occasion the total protein was 4 5 Gm (albumin 3 3 Gm and globulin 1 2 Gm)

Examination shows both thighs and legs to be indurated with a noninflammatory type of edema which pits on deep pressure The enlargement of the left is the greater of the two The skin of both legs shows slight thickening, with a little pigmentation and a few nodular infiltrations There appear to be constricting bands around the ankles There is slight pitting edema of the dorsa of both hands The face, especially around the malar bones, seems slightly puffy Some reduction of the swelling of the legs is noted on elevation

DISCUSSION

DR GEORGE C ANDREWS I am pleased to have seen this case because I have a patient with similar swelling of the legs of unexplained cause, but a study of the serum proteins has never been made It is interesting to me that this condition of the serum globulin exists I did not realize that people live without gamma globulin What was the interval in dates between the globulin determinations?

DR GERALD F MACHACEK Dr Combes noted a discrepancy in the determinations in different institutions

DR MAURICE J COSTELLO If one did not know the history of absence of serum globulin, one would almost think this patient had Milroy's disease She has lymphangiectases and fibrous nodules on the anterior tibial regions She had her first attack of erysipelas of the leg while she was in the hospital She has been quite free of infections of all types, I asked her whether she had ever had measles, and some one said her brother had the disease but the patient was given gamma globulin in the incubation stage and acquired measles in a mild form

DR GEORGE M LEWIS Will Dr Combes please outline the difference between this condition and Milroy's disease?

DR MAURICE J COSTELLO Apparently this patient's symptoms have remained exactly the same through the years, so one would not expect much change in the globulin estimations You will recall a case that I presented last year for Dr Wise, that of the baby of a physician who presented an unusual generalized edema not unlike that shown by this patient I shall advise the father regarding this case and suggest determinations of the gamma globulin

Sclerodactylia (?) Following Myocardial Infarction Presented by DR GERALD F MACHACEK

DISCUSSION

DR GERALD F MACHACEK I ran across an article by A H C Johnson in the *Annals of Medicine* (**19** 433-456, 1943) reporting a series of 178 consecutive cases of myocardial infarction, in 21 8 per cent of which the patient evidently presented this type of lesion In the same volume Kenneth C Kehl (pp 213-223) reported 6 cases of Dupuytren's contracture in the presence of myocardial infarction

Psoriasis Following Smallpox Vaccination in a Seven Year Old Boy Presented by DR GEORGE M LEWIS

A Case for Diagnosis (Ulcus Vulvae Acutum of Lipschutz?) Presented by DR ANTHONY C CIPOLLARO

T L, a woman aged 35, first consulted me on Nov 15, 1946, because of recurrent ulcerative vulvar and oral lesions of eighteen months' duration The lesions began as small blisters and soon ulcerated The patient has used a number of remedies, but the lesions have continued to recur A month before consulting me the patient went to the Lahey Clinic for a complete medical check-up Her general physical examination was entirely normal except for slight obesity and the lesions of the mucous membranes of the mouth and vulva The result of the Hinton test was negative, and all laboratory studies gave normal results A smear from the vagina contained a moderate number of gram-negative bacilli, a few gram-positive bacilli and extracellular gram-negative diplococci No intracellular gram-negative diplococci were seen Smears from the mouth showed a moderate number of fusiform bacilli and gram-negative bacilli There were also a few gram-negative diplococci A positive diagnosis was not made, but the following diagnoses were considered Vincent's angina, aphthous stomatitis, Behcet's triple symptom complex, erythema multiforme, dermatitis herpetiformis and pemphigus

When I first saw the patient she had discrete pinhead-sized to pea-sized, deep, ulcerative lesions on the mucous membrane of the labia minora and some in the posterior part of the fourchet The mucous membrane surrounding and underlying the lesions was painful, red and somewhat edematous A few ulcerative lesions, much smaller and less severe, were seen in the mouth, and the gums appeared to be inflamed The tongue and the roof and floor of the mouth were essentially normal On clinical grounds the diagnosis of ulcus vulvae acutum was made There was no biopsy

The patient was treated with antiseptic solution, penicillin ointment and acetarsone and showed quick response There has been a recent exacerbation of the gums, and the patient was given vitamin C and riboflavin

She is presented for diagnosis and for suggestions regarding therapy

DISCUSSION

DR. A BENSON CANNON I suspect that the case is one of pemphigus Pemphigus sometimes remains limited to the mucous membranes for many months, and it is difficult to diagnose before it becomes generalized For example, a patient was admitted to the Vanderbilt Clinic several months ago with a severe, widespread, bullous eruption, conjunctivitis and lesions in the mouth and pharynx and on the labia, and a diagnosis of bullous erythema multiforme of the Stevens-Johnson type was made She now has typical pemphigus vulgaris with vegetating lesions Dr Cipollaro's patient is similar to the one I presented this afternoon The lack of pain and the number of lesions are against the diagnosis of ulcus vulvae acutum

DR FRED WISE It is difficult to make a definite diagnosis in cases of this kind, unless one has the opportunity of keeping the patient under observation for a long time Patients with a diagnosis of ulcus vulvae acutum sometimes have

DR HOWARD FOX At first glance this swelling looked like a paraffinoma It is a lymphedema of unknown origin, and I do not believe that anything can be done for it

DR MAURICE J COSTELLO I think that this patient should be studied thoroughly A focus of infection may be found in the sinuses During the course of the examination there was a constant seropurulent discharge from the nose, and I think temporary improvement might be obtained by the administration of sulfonamides, especially sulfathiazole I suggest a trial of streptomycin

DR A BENSON CANNON The lesions in this case remind me more of granuloma inguinale than any other condition that I am acquainted with, and I should investigate the case with that diagnosis in view I should also perform a Frei test and have a hematologist study her leukocytes and, perhaps, take a bone marrow specimen

DR GEORGE C ANDREWS I suspect a diagnosis of solid edema of the face I was also thinking of leukemia because some of the infiltration suggests that diagnosis, and hypertrophic gingivitis may occur in leukemia

Tinea Capitis (Microsporum Lanosum) in Mother and Son Presented by DR ANTHONY C CIPOLLARO

Syphilis (or Tuberculosis Cutis of a Buttock?) Presented by DR GEORGE C ANDREWS

Balanitis Xerotica Obliterans Presented by DR A BENSON CANNON

N T, a man aged 37, first consulted me on June 14, 1947, complaining of phimosis and preputial fissuring, which began fourteen months previously The lesions began with small erosions or fissures on the frenulum praeputii penis which occasioned slight stinging on micturition Healing of the erosions was followed by the development of a grayish white, scarlike process which gradually increased to form a band about the prepuce Retraction of the prepuce has become increasingly difficult, and its performance causes fissures to appear

Examination shows a compact, well built man whose blood pressure is 128 systolic and 90 diastolic He has a fairly well advanced temporal thinning of the hair The prepuce is long and presents numerous superficial radial fissures There is a dense bandlike thickening about the circumference of the prepuce extending to the frenulum praeputii penis and the urinary meatus The thickened areas have a dull, gray-white appearance The urinary meatus seems narrowed Much smegma is present in the preputial sac

The basal metabolic rate was —11 2 per cent The Mazzini reaction of the blood was negative on two occasions The blood arsenic level was 0 32 mg per 10 Gm of dried blood

With the use of a simple protective paste the fissure of the prepuce healed promptly and retraction ceased to be painful though the cicatricial changes persisted In August 1947 treatment with vitamin E (eprolin-S®) was begun in doses of 5 Gm three times daily Despite this, the tightness of the prepuce increased, and by October retraction could be accomplished only with the assistance of soaping and considerable traction On October 28 treatment with tripelennamine hydrochloride (pyribenzamine hydrochloride®) was begun with 200 mg daily, increasing to 400 mg a day Use of vitamin E was also continued After three weeks on this regimen the patient felt that he had initially shown some improvement but that the process was stationary at that time

A Case for Diagnosis (Lichen Planus? Lupus Erythematosus?) Presented by Dr Maurice J Costello

Hereditary Hemorrhagic Telangiectasia with Hemangioma Presented by Dr John N Graham

A Case for Diagnosis (Lichen Planus Hypertrophicus? Amyloidosis?) Presented by Dr Anthony C Cipollaro

Psoriasis Exacerbation Following Vaccination Presented by Dr George M Lewis

B O, a woman aged 23 from New York Hospital, has had psoriasis since the age of 6, limited to the elbows, scalp and sacral region, with mild exacerbations and remissions Five weeks ago she was vaccinated, and three days later numerous small psoriasiform lesions developed on the trunk, face, neck and extremities A confluent nummular patch of psoriasiform lesions appeared at the vaccination site, and the long-standing patches on the elbows and scalp became larger One sister also has psoriasis

There are numerous dime-sized to quarter-sized erythematous scales distributed over the face, neck, trunk and extremities The vaccination area shows a dollar-sized psoriasiform patch The Mazzini reaction of the blood was negative The results of biopsy were compatible with acute psoriasis

DISCUSSION

Dr George M Lewis This is the third patient we have seen with an acute attack of psoriasis developing immediately after vaccination Since the cause of psoriasis is not known, one could consider that in some way the virus infection had had a specific effect on the disease

Lichenoid Miliary Sarcoid Presented by Dr Maurice J Costello

A Case for Diagnosis (Pemphigus?) Presented by Dr A Benson Cannon

Vaccinia, Generalized, Following Vaccination for Smallpox Presented by Dr A Benson Cannon

Leprosy, Lepromatous Type, with Tufted Destruction of the Tips of the Terminal Phalanges Presented by Dr Maurice J Costello

B O, a man aged 20, a Puerto Rican, is presented from Willard Parker Hospital, to which he was transferred from Harlem Hospital He had sought attention at the latter institution on March 13, 1947, because of pain in the right groin, severe nausea and vomiting Intestinal obstruction was considered on admission, but the gastrointestinal symptoms subsided with conservative treatment

While the patient was in Harlem Hospital, a cutaneous eruption was noted, although his skin was reported to have been clear on admission He had noted scaling of the feet in October 1946 No one in the family has a similar eruption and there has been no known contact with leprosy The patient has been in the United States for about eight months

Society Transactions

SAN FRANCISCO DERMATOLOGICAL SOCIETY

Ervin Epstein, M D, *President*
Frances M Keddie, M D., *Secretary-Treasurer*
April 26, 1946

A Case for Diagnosis (Thymoma). Presented by DR FRANCES A TORREY

Lymphoblastoma. Presented by DR FRANCES A TORREY

Lupus Erythematosus (Lichen Planus?) Presented by DR HIRAM E MILLER

C F S, a 56 year old white man, was first seen in the Dermatology Clinic of the University of California Hospital on Jan 7, 1946 He gave a history of a reddish scaly dermatitis on the face and neck for the past seventeen or eighteen years and of elevated purplish nodules on the backs of the hands for about one year

The physical examination revealed no abormalities A blood cell count and urine were reported normal The Kolmer and Kahn reactions were negative A fairly symmetric erythematous and scaly eruption involves the ears, nose and sides of the neck Whitish retiform lesions are present on the buccal mucosae, and the lips showed some deformity from atrophic scarring On the dorsa of the hands are groups of large, elevated, flat-topped and rounded violaceous papules

Biopsy specimens were obtained from the dorsum of the left hand and from the side of the neck Studies of a section from the neck showed slight parakeratosis and relative acanthosis The granular layer was prominent, and the basal cell layer of the rete pegs showed some liquefaction degeneration A fairly dense round cell infiltrate was present and was confined to the papillae and upper part of the cutis

The section from the dorsum of the hand showed prominent hyperkeratosis and an increased granular layer There were decided acanthosis with some liquefaction degeneration of the basal cell layer A moderately dense round cell infiltrate was present in the papillae and upper part of the cutis

Bismuth subsalicylate was given, 0 2 Gm intramuscularly weekly for a total of sixteen injections During this period there has been gradual regression of all cutaneous lesions

DISCUSSION

DR ERVIN EPSTEIN I had the opportunity of seeing this patient ten years ago in Los Angeles At that time he had typical lupus erythematosus on the nose and lips and no other lesions

DR. F G NOVY JR I agree with the diagnosis of lupus erythematosus

DR REES B REES I think that someone should point out the remarkable bandlike infiltrate in the sections from the hand and neck and the prominent

DR ANTHONY C CIPOLLARO I agree with the presenting diagnosis I think that too often patients with leukoplakia are given a serious prognosis Carcinoma does develop in patches of leukoplakia, but it is of rather infrequent occurrence, and people interested in the cancer problem lead us to believe there must be a definite sequence from leukoplakia into cancer, which I think is erroneous I recently saw a physician with extensive lichen planus all over the body, with extensive lesions on the buccal mucosa, including the border of the lip, and on the vocal cords, causing him to be hoarse They could be seen distinctly with the laryngeal mirror I have never seen or read of lesions of lichen planus on the vocal cords

DR GEORGE C ANDREWS I think that fear of leukoplakia is well warranted by the fact that often when it does become cancerous the lesion is extremely serious and by the fact that one never knows in a case of leukoplakia whether cancer cells are present or not One may take a biopsy specimen from one portion of the leukoplakia and histologically find only leukoplakia and then cut some more sections and find cancer So it is a serious disease, and I believe that lichen planus of the mouth is also a serious disease, especially if it lasts over some time I have had 2 patients with lichen planus of the buccal mucosa in whom cancer of the buccal mucosa developed after the lesions had been present for twenty years It is certainly a precancerous disease I do not think that the fact that this man has lichen planus means that he has nothing to worry about The patient should be treated and should be watched, told to stop smoking and given vitamin B complex and whatever other therapy may be available

DR JOHN C GRAHAM I agree with the diagnosis It seems to me that the lesion on the tongue was rather typical of a healing lichen planus

DR HOWARD FOX I had occasion to write up a series of 10 cases of lichen planus confined to the mouth One of the patients, a man whom Dr Udo Wile had seen, was a great smoker and for eight years had had attacks of lichen planus that flared up after smoking, when he stopped smoking the eruption quieted down

DR GEORGE M LEWIS I believe, as Dr Andrews does, that a patient with lichen planus of the buccal mucosa should stop smoking, and the patient was so advised He was given a bland mouthwash but no other treatment because my results have been rather poor in treating lichen planus of the buccal mucosa

Edema Due to Hypoproteinemia Presented by DR FRANK C COMBES

D E, a white girl aged 16, was admitted to Bellevue Hospital complaining of long-standing swelling of both legs It was noted a few days after birth, but it was not known whether it was confined to the legs The patient states that the swelling disappeared spontaneously from the age of 2 years until she was 8 When at the age of 9 or 10 years the swelling recurred, she entered Mount Sinai Hospital, where extensive studies were done and reported (Schick, B, and Greenbaum, J W Edema with Hypoproteinemia Due to Congenital Defect in Protein Formation [Case Report], *J Pediat* **27** 241-245 [Sept] 1945) After her discharge the swelling of the legs remained stationary with no accompanying fever, inflammation or tenderness In 1946 she reentered Mount Sinai Hospital twice, blood plasma transfusions were given with but temporary relief, the swelling would go down for two days and then recur Her most recent admission to Mount Sinai Hospital took place in the summer of 1947 At that time, in addition to the usual swelling of the extremities, there was edema of the face, back and abdomen She was treated with sodium and potassium acetate, as a result of which the condition of all but the legs returned to normal The edema of the legs has persisted

DR HIRAM E MILLER In general, I believe that these patients will be seen by the psychiatrist for a visit or two, and then they will come back to the dermatologist If their delusions are well established, little can be done for them by the psychiatrist or the dermatologist

DR E J RINGROSE (by invitation) Favorable results have been achieved with patients with dermatitis factitia who would submit themselves to interview Most of the patients, under the influence of sodium amytal® (sodium isoamylethylbarbiturate) given intravenously, will admit what they have been using

DR MERLIN T-R MAYNARD, San Jose, Calif One of the patients admitted the use of needles and pincers Her euphoric personality fits into the diagnosis readily The other one started talking about herself and her troubles immediately, which fits into the picture of a neurosis of the neurotic excoriation type, a typical picture Nodules particularly can be produced by a traumatic agent We all see children pick and squeeze their skin, but it does not result in hemorrhage into the areas

DR ERVIN EPSTEIN I realize that the condition in such cases is usually diagnosed as dermatitis factitia, and I am willing to accept that diagnosis for these patients However, I am unable to see how the primary subcutaneous nodules could be produced mechanically

A Case for Diagnosis (Bacteremia?) Presented by DR FRANCES A TORREY

A Case for Diagnosis (Dermatitis Medicamentosa?) (Purpura Annularis Telangiectodes?) Presented by DR FRANCES M KEDDIE

V D C, a 47 year old Portuguese woman, was first seen in the University of California Dermatology Clinic in March 1945, at which time a diagnosis of black hairy tongue was made No cutaneous eruption was present at that time

On April 1, 1946, she returned to the clinic because of lesions of both legs of about ten months' duration There are numerous pigmented purpuric macules of various sizes and shapes Many of these lesions show telangiectasia The patient states that she had taken "sleeping pills" regularly for many years The physical examination revealed no abnormalities

Laboratory examination revealed 4,400,000 erythrocytes, 90 per cent hemoglobin and 8,900 leukocytes, the differential count was normal The sedimentation rate was 11 mm in 1 hour The capillary clotting time was 8 minutes The tourniquet test at a pressure of 80 mm of mercury for 15 minutes caused numerous petechiae The prothrombin time was 80 per cent The urine was normal

Microscopic sections showed increased deposition of pigment in the basal cell layer and occasional deposits of hemosiderin in the cutis Extravasation of red blood cells and hyalinization of several vessel walls were noted A perivascular infiltrate consisting of lymphocytes and polymorphonuclear leukocytes was present

DISCUSSION

DR NORMAN EPSTEIN This case suggests Majocchi's disease

DR STUART WAY A diagnosis of dermatitis medicamentosa is in order, but not Majocchi's disease This case has none of the characteristics of purpura annularis telangiectodes in the cases that I have reported

DR HIRAM E MILLER This is a good example of purpura, but not of purpura annularis telangiectodes There is no definite annular appearance, and there are no telangiectases It may be a toxic purpura, but not Majocchi's disease

This patient seems to be acquiring that condition as well It could be explained on the basis of anoxemia Going into the possibility of whether the condition was due to the coronary sclerosis, Johnson came to the conclusion that it probably is a cardiac pain reflex because of the peculiar connection between the first thoracic segment and the lower cervical and upper thoracic sympathetic ganglions, causing reflex constriction of the vessels of the hands "Trophic" ulcers of the hands following coronary disease also occur

A Case for Diagnosis (Bullous Lupus Erythematosus?) Presented by DR MAURICE J COSTELLO

A Case for Diagnosis (Dermatitis Medicamentosa? Mycosis Fungoides?). Presented by DR HOWARD FOX

Epidermal Cyst on the Finger Presented by DR MAURICE J COSTELLO

Dermatitis Herpetiformis and Lupus Erythematosus Occurring Consecutively and Simultaneously in a Patient Who Had Had Splenectomy for Purpura Hemorrhagica Presented by DR MAURICE J COSTELLO

George M Lewis, M D, *President*
John C Graham, M D, *Secretary*
Dec 16, 1947

Acnitis Presented by DR A BENSON CANNON

A Case for Diagnosis (Ulcus Vulvae Acutum? Triple Symptom Complex of Behcet?) Presented by DR A BENSON CANNON

Chronic Lymphedema of the Face, Hypertrophic Gingivitis, Rosacea Presented by DR ANTHONY C CIPOLLARO

A S, a woman aged 45, first noticed swelling of the upper lip, nose and right side of the face eleven years ago, with less involvement of the left side of the face These episodes of swelling were thought to be due to some infection of the teeth, but multiple extractions yielded no improvement The patient suffered an attack of Bell's palsy on the right side about ten years ago, accompanied with a severe exacerbation of the facial swelling on the affected side, and this has continued more or less unabated up to the present The condition is greatly aggravated by exposure to cold or dampness

The patient presents a nonpitting, moderately firm, edematous swelling of the cheeks, nose and right periorbital tissues The right side of the face shows the greater involvement In addition, there is a papular eruption of the nose and cheeks with moderate erythema of the affected areas The gingivae are greatly swollen

DISCUSSION

DR RAY H RULISON I have never seen that type of gingivitis The patient said that her dentist had taken roentgenograms of those teeth and found them perfectly sound I thought that the swelling of the gum was related to the lymphedema

sort of poikiloderma I do not know whether it is melanosis of Riehl or poikiloderma of Civatte or whether it is primarily an abnormal reaction to light and to tar and oil I think that Dr Fasal is able to tell us more about melanosis of Riehl since he worked in the Riehl clinic, with both the elder and the younger Riehl

DR PAUL FASAL I think that this is a case of melanosis, but not melanosis of Riehl Riehl included in his description only cases due to ingestion of toxic products Those cases were seen after World War I when people used various food substitutes containing toxic products I consider this disease a tar melanosis, but not melanosis of Riehl

DR F G NOVY JR In a generalized Berloque dermatitis there is the same problem of perfumes plus sunlight This woman is probably a sensitive person who has been exposed to various tar products and sunlight and has reacted with the formation of pigment

DR HIRAM E MILLER I agree with Dr Fasal It is melanosis, but not melanosis of Riehl or poikiloderma Dr Templeton made the statement that he thought it was melanosis of Riehl or poikiloderma and that there was a question of industrial liability I believe that if either of these two diagnoses were accepted, there would be no question about industrial responsibility The distribution of lesions here is not that of melanosis of Riehl, because, as I understand it, the scalp is always involved in this disease In this patient the scalp is not involved The patient has no involvement around the breasts and in the axillary folds as is usually observed Melanosis of Riehl is of toxic origin, while in this patient the causative factor is tar and oil plus sunlight For these reasons I believe that it is melanosis, but not melanosis of Riehl

DR HARRY J TEMPLETON I agree with Dr Novy that this is due to action of tar or oil on skin which has become sensitized to sunlight

DR REES B REES According to the textbooks, in tar melanosis the distribution is confined to face, scalp, shin, hands and forearms There is pigmentation, but telangiectasia or atrophy is not mentioned The patient has telangiectasia

DR MERLIN T-R MAYNARD, San Jose, Calif The fact that the patient is a machine operator should be considered Hot tars and oils become volatile Considering the fact that tar could have been ingested through three channels, the skin, the respiratory tract or the mouth, it is possible that she has ingested a certain amount of it through the respiratory system The traps of respirators demonstrate that one eats what one breathes This could therefore be melanosis of Riehl in the classic sense

Ervin Epstein, M D, *President*

Frances M Keddie, M D, *Secretary-Treasurer*

Sept 13, 1946

Pemphigus of the Conjunctiva Arsenical Pigmentation and Keratoses from Fowler's Solution. Presented by DR OTTO E L SCHMIDT

Angiokeratoma? Presented by DR OTTO E L SCHMIDT

Subcutaneous Granuloma Annulare Presented by DR HIRAM E MILLER

T H S, a four year old white boy, was first seen in the University of California Hospital on July 9, 1946, with a chief complaint of multiple nodules

DISCUSSION

DR EUGENE F TRAUB Dr Cannon gave this patient pyribenzamine,® and to the best of my knowledge it has not been used in this disease before, although patients with scleroderma show considerable benefit from its use Certainly Dr Cannon has helped this patient and that is to be remembered, as it is the first drug that has influenced this disease, as far as I know

DR HOWARD FOX I suggest circumcision and think that it would relieve the whole trouble The little band is in the foreskin

DR A BENSON CANNON I am under the impression that a number of cases have been reported in which this condition is said to have followed circumcision and that one should avoid that operation, if possible, under these conditions This patient had symptoms suggestive of endocrine disturbance, such as sweating of the palms, rapid pulse and other emotional disturbances and a basal metabolic rate of —12 per cent It was because of these symptoms that we prescribed diphenhydramine (benadryl®) He had had large doses of vitamin E uninterruptedly for four months without any change in his condition

A Case for Diagnosis (Carcinoma of the Mouth? Gumma of the Mouth?) Presented by DR ANTHONY C CIPOLLARO

A Case for Diagnosis (Sarcoid?) Presented by DR GEORGE M LEWIS

A Case for Diagnosis (Sarcoid? Syphilis) Presented by DR MAURICE J COSTELLO

Syringoma Presented by DR GEORGE M LEWIS

DR REES B REES A guinea pig inoculation was done at the Permanente Hospital, but the result was not reported to us Necrobiosis lipoidica diabeticorum resembles this disease histologically, but the comparison ends there

A Case for Diagnosis (Actinic Dermatitis? Lupus Erythematosus?) Presented by DR REES B REES

Carotenemia Presented by DR H V ALLINGTON

A Case for Diagnosis (Monilethrix?) Presented by DR H V ALLINGTON

Generalized Progressive Scleroderma Presented by DR WILLARD M MEININGER

A Case for Diagnosis (Progeria? Lupus Erythematosus?) Presented by DR FRANCES M KEDDIE.

D A B, a 6 year old white girl, was first seen in the University of California Dermatology Clinic on Aug 12, 1946 Dermatitis has been present on the face since the age of 6 months One year ago she sustained second degree burns of her arms and back which required skin grafting In the pediatric clinic a diagnosis of microcephaly, dwarfism and congenital heart disease was made

At the present time there is a rather diffuse blotchy erythematous scaly eruption with scarring and atrophy involving the nose and cheeks There are numerous, discrete, erythematous, papular and excoriated lesions on the extremities The lids are reddened and crusted and the conjunctivas injected Her height, weight and skeletal measurements are below normal for her age

There were no abnormal observations in laboratory studies of the blood, urine, glucose tolerance and urine porphyrins The tuberculin cutaneous reaction was negative

DISCUSSION

DR HARRY J TEMPLETON I presented the same patient with the same diagnosis at one of our previous meetings My co-workers and I have studied this case at the Children's Hospital in Oakland and wound up just where we started Not only was there some abnormal delay in the general development of the child, but of the skull, the heart and the child's skin, and for lack of a better classification it was called progeria I cannot say that the lesions have made much progress or retrogression, they are still in status quo The child is not microcephalic, she is rather bright for her age

DR W F HARDING (by invitation) We do not feel that this disease quite fits into the picture of progeria The child does not show atrophic changes in the skin She has no loss or graying of hair or arteriosclerosis Talbot of Harvard has studied a number of cases of progeria The results of all metabolic studies made in these cases were within relatively normal limits Talbot and his co-workers came to the conclusion that in cases studied the caloric intake and output was more or less in equilibrium, all the heat and energy being expended without anything being left over for body development Most patients showed greatly increased metabolism without hyperthyroidism

follicular plugging in the epidermis There are some plasma cells in addition to small round cells

DR HARRY J TEMPLETON The lesions on his hands are deep violaceous and are thickened They are classic lesions of lichen planus hypertrophicus There may be two conditions

DR NORMAN EPSTEIN It is of interest that biopsy specimens from the hands and neck in this case are much alike Although the bandlike infiltrate in the upper part of the corium suggests lichen planus, the lesions on the face could hardly be anything but lupus erythematosus

DR ARNE E INGELS I agree, the sections verify that

DR HIRAM E MILLER I examined sections from this patient and made a diagnosis of lichen planus, but after examining the patient I feel reasonably certain that he does not have this disease The microscopic observation must be correlated with the clinical picture The patient certainly has lupus erythematosus on the face, and the lesions on the dorsa of the hands resemble lichen planus but could be, and probably are, lupus erythematosus The sections showed an increase in the granular layer, and the infiltrate was certainly bandlike The histologic changes are compatible with the diagnosis of lupus erythematosus, and the clinical appearance, I think, is also that of lupus erythematosus

A Case for Diagnosis (Necrotic Nodules on the Face?) Presented by DR ERVIN EPSTEIN

DISCUSSION

DR G V KULCHAR The diagnosis for the older woman of the 2 patients, I think, is factitious dermatitis, which is especially apparent from the linear scarring The disease of the other woman might be what is called pyoderma faciale

DR REES B REES I believe that both women have neurotic excoriations The case that Dr Kulchar discussed first is interesting and classic, because of the patient's elaborate description of the manipulation of her lesions

DR MERLIN T-R MAYNARD, San Jose, Calif I agree with the diagnosis of neurotic excoriations Both women admit picking and squeezing their skin The scars are typical of those produced by persistent manipulation I tried the pharyngeal reflexes in each of them Each has a rather active pharyngeal reflex

DR. ERVIN EPSTEIN The diagnosis of dermatitis factitia presupposes a method of producing the lesions These lesions started subcutaneously as hard nodules There is no question that the lesions have been altered mechanically, but I still find it difficult to believe that the lesions could be produced by any chemical, physical or mechanical agent

DR E J RINGROSE (by invitation) I think that these excoriations were produced by finger nails I believe that one should differentiate between neurotic excoriations, of which the lesions in these cases are typical, and dermatitis factitia produced by chemical or other destructive agents Have you not seen a primary lesion produced by pinching and squeezing?

DR E K STRATTON I think that these patients can be helped by a psychiatrist if they wish to be helped However, most of them are not willing to cooperate I believe that in any event they belong in the office of a psychiatrist and not in the office of a dermatologist

be a superimposed infection of some sort I think that it would be worth while to look for Frisch bacilli I could not find any record of such examinations having been made here The patient is apparently in good general health, despite the extensive lesions on his nose

DR PAUL FASAL This case reminds me of 2 cases of rhinosporidiosis which I have seen I would suggest the use of antimony potassium tartrate as a therapeutic experiment

DR HARRY J TEMPLETON I thought that it was a typical vegetative lesion of bromide or iodide dermatitis

DR JAMES DRAKE While in Japan, this soldier drank almost entirely from Lister bags The possibility of the unauthorized use of an iodide as a water purifier occurs to me Has the question of iodide ingestion been investigated?

DR E K STRATTON If this eruption were in the groin I would think of granuloma inguinale I have seen cases of this disease in the groin with subepidermal pustules as well as the granulomatous lesions similar to what this case presents I agree with Dr Fasal that antimony therapy should be tried

LIEUTENANT COLONEL ROBERT S HIGDON (by invitation) Rhinoscleroma was suspected, and I have tried to demonstrate the causative agent of that disease by smears, cultures and biopsy sections, but have been completely unsuccessful thus far Bromides and iodides were also considered, and the patient was given tests accordingly, but these tests have also been without positive results

Thymoma Presented by DR FRANCES A TORREY

Ervin Epstein, M D, *President*

Frances M Keddie, M D, *Secretary-Treasurer*

Nov 15, 1946

Balanitis Xerotica Obliterans Presented by DR E A LEVIN

A Case for Diagnosis (Behcet's Syndrome? Pemphigus?) Presented by DR JOHN M GRAVES

Multiple Neuromas of the Skin Presented by DR ERVIN EPSTEIN

J W, a 24 year old white man, presents a nodular eruption below the right lower lid, on the lid and on the margin The lesions consist of shiny, smooth, flesh-colored discrete and coalescing nodules They are firm Some of the older lesions show hyperkeratosis of the surface, possibly due to previous therapy

The disease started ten years ago, after an injury The patient stated that when he arrived home some "goose pimples" were present below his right eye and that these have enlarged and slowly spread during the past ten years The lesions are asymptomatic

Treatment has included "freezing," one year ago, "burning with an electric needle," one month later, and the use of "acid" by the patient on numerous occasions since This has failed to eradicate the lesions or to stop the development of new ones

DR FRANCES M KEDDIE When the patient was first seen the lesions were annular and telangiectatic, now they are purpuric and diffuse Tonight she stated that she had been taking "sleeping pills" for one year only This eruption is certainly of not more than one year's duration and may be a toxic reaction to self medication

Dissecting Cellulitis of the Scalp (Perifolliculitis Capitis Abscedens et Suffodiens) Presented by DR GRANT MORROW

A Case for Diagnosis (Psoriasiform Eruption? Lymphoblastoma?) Presented by DR FRANCES A TORREY

A Case for Diagnosis (Keratosis Palmaris et Plantaris Associated with Carotenemia? Pityriasis Rubra Pilaris?) Presented by DR H V ALLINGTON

Hodgkin's Disease and Cutaneous Torulosis Presented by DR FRANCES A TORREY (previously presented by DR TORREY at the April 1945 and October 1945 meetings of the San Francisco Dermatological Society)

A Case for Diagnosis (Localized Scleroderma?) Presented by DR NORMAN EPSTEIN and DR. JULES KEY (by invitation)

A Case for Diagnosis (Melanosis of Riehl?) Presented by DR H V ALLINGTON

V G, a white woman aged 46, was seen first on April 11, 1946 She presented a brownish pigmentation of the face, the neck, the exposed portion of the upper part of the chest and to a lesser degree of the arms The skin also showed irregular telangiectasia and erythema and on the cheeks was shiny and glazed The patient stated that this condition had been present a little over two years

The patient attributed this to exposure to the fumes from hot lubricating oils in her work for an oil company Her work consisted in running viscosity tests and gaging tanks of hot oil She had done this work for about four years She stated that exposure to the fumes from the hot oil caused her skin to burn and sting and become "purplish pink" After work, cool applications were required to quiet the burning sensation Recently she used vinegar for relief She had not done anything previously about her problem because she was anxious to hold her job, which she liked She had also noticed that exposure to sunlight caused increased redness, burning and stinging However, her work was indoors, and exposure to light was kept at a minimum She further stated that exposure to the fumes of heavy oils was more irritating than to that of light oils

She is for the most part a vegetarian She does not eat carrots or other carotene-containing foods to excess, however, and the character of her pigmentation is not that of carotenemia

I believe that this patient is one who is sensitive to the fumes from hot oils and that her reaction is primarily on this basis An endocrine or dietary deficiency may be present and may increase the sensitivity of her skin

DISCUSSION

DR HARRY J TEMPLETON I saw this patient with Dr Allington, and at that time there was a question of industrial liability The patient has some

A Case for Diagnosis (Psoriasis? Lichen Planus?) Presented by DR REES B REES

Xanthoma Diabeticorum Presented by DR PAUL FASAL

A Case for Diagnosis (Endothelial Tumor? Angioblastoma?) Presented by DR HARRY E ALDERSON and DR CHARLES ALBERT SHUMATE

C W, a white man aged 66, presents a well outlined, dark blue patch, 4 cm in diameter, superior and posterior to his left eye Surrounding this area and extending over most of the left cheek is a hard, somewhat puffy, violet discoloration (ecchymosis) The areas are painless On the anterior frontal region are two crusted keratotic lesions There is ptosis of his left lid His serologic test for syphilis gave negative reactions

A report from Dr Ream Leachman, of Vallejo, stated that Dr Medley, an oculist, examined the patient's eyes and reported that the lesions of the left lid were noninflammatory and that the ptosis was from their weight The eyeball was normal The vision, orbital contents and fundi were normal

As we believed that the disease might be the result of neurotrophic changes in the trigeminal area, for example, due to thrombosis of the posterior inferior cerebellar artery, the patient was referred to Dr Edmund Morrisey (neurosurgeon) for consultation He reported that there were no neurologic changes of significance

The histologic sections were examined by Dr Wilbert Sachs, of New York He reported that throughout the middle and upper parts of the cutis in one portion of the slide were numerous blood vessels and spaces and an intense cellular infiltration of angioblasts The surrounding tissue and overlying epidermis showed no important change The cells had large round, fairly well stained nuclei and either no cytoplasm or only a slight amount The diagnosis from microscopic study was some type of endothelial tumor, belonging to the angioblastoma group

Favorable Response of Tuberculosis Cutis (Lupus Vulgaris) to Therapy with Vitamin D Presented by DR REES B REES

A Case for Diagnosis (Multiple Areas of Superficial Atrophy of the Trunk Macular Atrophy?) Presented by DR H V ALLINGTON

Coccidioidal Granuloma on the Cheek Presented by DR OTTO E L SCHMIDT

A Case for Diagnosis (Generalized Papular and Nodular Eruption Present at Birth) Presented by DR H V ALLINGTON

C M C, a 4 month old Negro baby girl, except for her skin, was a normal full term infant weighing 5 pounds 8 ounces (2,495 Gm) She has grown and developed in an average manner She has one normal 3 year old sister There is no history of similar cutaneous trouble in her family

At birth she presented a generalized papular and nodular eruption, with lesions varying in size up to 1 5 cm in the largest diameter These were firm

on the legs and back of the head of about eight months' duration A history of a fall prior to their appearance was obtained, but subsequently more nodules developed without preceding trauma

Positive physical observations include nontender firm fixed nodules on the left occipital region, larger purplish nodules on the right tibia and similar smaller nodules on the left knee There is generalized nontender moderate adenopathy Routine tests revealed that the blood and urine were normal The reaction to an intracutaneous tuberculin test, in dilution of 1 1,000, was negative The reaction to the coccidioidin test, in dilution of 1 1,000, was negative The blood cholesterol was 112 mg per hundred cubic centimeters Serum protein was 6 mg per hundred cubic centimeters (albumin 3 8 Gm and globulin 2 2 Gm) Serum calcium was 12 mg and serum phosphorus 4 48 mg per hundred cubic centimeters Phosphatase was 6 2 Bodansky units Roentgenograms of the chest and long bones showed no abnormalities Biopsy of the marrow revealed a normal differential count Microscopically the sections of a nodule showed a focus of coagulation necrosis of the connective tissue surrounded by radiating strands of fibroblasts, epithelioid cells and lymphocytes in palisade arrangement (Starting Aug 20, 1946, both cutaneous lesions were irradiated, a total of 200 roentgen rays was used with a 3 mm filtration of aluminum)

DISCUSSION

DR RHEA B REES I saw this patient on the ward with Dr Miller, Dr Keddie and other members of the staff At that time we thought of sarcoid, having just the clinical appearance to go on The lesion on the left knee was clinically suggestive of granuloma annulare, but we did not think of that diagnosis until the histologic section was studied Dr Brown found an interesting article by Udo Wile on this subject

DR MARSHALL BROWN (by invitation) This article appeared in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY (**30** 785, 1934), a report of an unusual case of granuloma annulare by Dr F G Graver and Dr Udo Wile, of the University of Michigan Medical School The first reports were in 1908 by a British writer, Dr Graham Little He reported several cases of possible subcutaneous granuloma annulare The next reports were written in 1931 by Jacobi (Jadassohn, J Handbuch der Haut- u Geschlectskrankheiten, Berlin, Julius Springer, 1931, vol 10, p 796) He reported several cases of subcutaneous granuloma annulare which occurred on the palms and the flexor surfaces of the fingers, and the dorsal surfaces of the feet and lower extremities However, there were no case reports at that time of subcutaneous granuloma annulare occurring in the scalp The case reported by Dr Wile occurred in a 2 year old white boy who was admitted to the hospital with a history of subcutaneous nodules on the scalp, the flexor surface of the left wrist and the extensor surface of the right tibia Our patient's mother stated that the first time she noted nodules on the flexor surface of the wrist was five months prior to the patient's entrance into the hospital Three months before admission she noted five nodules occurring in the subcutaneous tissues of the scalp, and two months before admission she noted nodules occurring on the extensor surface of the right tibia Physical examination revealed subcutaneous nodules which were firm and attached to the underlying tissue, and the overlying skin was loose and movable There was no previous history of tuberculosis Members of the family were examined for tuberculosis, no evidence of this disease was found In the hospital the patient was asymptomatic

DR E K STRATTON Have a tuberculin test and guinea pig inoculation been done?

A Case for Diagnosis (Behcet's Syndrome? Pemphigus?). Presented by DR JOHN M GRAVES

V H, an American woman aged 52, was presented at the meeting of the San Francisco Dermatological Society on Nov 15, 1946

Verrucous Lupus Erythematosus? Nevus Verrucosus? Presented by DR STUART C WAY and DR JAMES R DRAKE

Lupus Erythematosus, Accentuated by Solar Sensitivity. Presented by DR ARNE E INGELS

Tuberculosis Verrucosa Cutis Presented by DR STUART C WAY and DR JAMES R DRAKE

Keratoderma of Buttocks (Syphilitic or Pyogenic? Psoriatic?) Presented by DR WILLARD M MEININGER

Maduromycosis Presented by DR HIRAM E MILLER

Subcutaneous Granuloma Annulare? Presented by DR HIRAM E MILLER

S S is a 4 year old girl Her mother stated that seven months previously she noticed a small lump under the skin on the lower part of the patient's right leg and on the extensor surface of the right elbow These areas have become progressively larger in size

The physical examination reveals two rather diffuse, cherry-sized, firm, subcutaneous nodules, not freely movable and nontender, with no overlying cutaneous changes, located on the extensor area of the right elbow and on the anterior surface of the lower part of the leg

In July 1946 roentgen ray examinations showed no pathologic bony changes in the right tibia and fibula, the right elbow and forearm or the skull In September 1946 there was noted increased density in the soft tissues of the right elbow The density was sharply outlined and homogeneous and appeared to conform to the position of the supinator muscle No evidence of abnormality was seen in the bones of the forearm In the roentgenograms of the right tibia and fibula there was a localized swelling of the soft tissue situated anteriorly over the tibia, in the region of the junction of the upper and middle thirds, but the bone structures of the tibia and fibula were normal In November 1946 there was increase in the size of the mass on the anterior superior surface of the right tibia The density in the left elbow was less definite

Agglutination reactions for brucellosis were negative The tuberculin cutaneous test gave a negative reaction The sedimentation rate was 8 mm per hour The hemogram showed 4,450,000 erythrocytes and 5,100 leukocytes, with neutrophils 10 per cent, lymphocytes 86 per cent and monocytes 4 per cent

On Dec 4, 1946, a biopsy was performed on the nodule of the right leg The specimen consisted of an incised piece of yellowish gray tissue of elastic consistency with some surrounding connective tissue It measured 1 4 by 1 2 by 0 9

Adenoma Sebaceum Multiple Sebaceous Cysts with Hypertrophy and Hyperplasia of Sebaceous Glands Presented by DR JOHN M GRAVES

A Case for Diagnosis (Pemphigus Vegetans?) Presented by LIEUTENANT COLONEL ROBERT S HIGDON, Medical Corps United States Army, Letterman General Hospital, San Francisco (by invitation)

J R, aged 34, while stationed in Tokyo, noticed slight intermittent epistaxis on April 15, 1946 Examination revealed a pinhead-sized creamy white papule ½ inch (1 27 cm) within the right nares on the lateral wall The papule grew rapidly and, within one week, had reached the size of a bean and was verrucous in appearance Within two weeks continued growth caused partial obstruction of the right nares At this time a second whitish pinhead-sized papule was noted just inside the left nares on the medial wall He was given treatment with sulfonamide drugs By the third week, the right nares was completely occluded and the second lesion had grown so rapidly that the left nares was partially occluded He was admitted to the 42d General Hospital in Tokyo, on May 6 Treatment with sulfonamide drugs was discontinued The verrucous growths were removed from both nares with electric cautery Within a week the lesions reappeared, accompanied with signs of secondary infection Results of dark field examination, biopsy, smears, cultures and serologic and blood tests were negative The lesions rapidly regenerated, completely obstructing both nares, and extended externally to involve all surfaces of the lower portion of the nose for a distance of 1 cm The patient was given one hundred and nine intramuscular injections of penicillin (40,000 units each) for a total of 4,360,000 units While he was receiving penicillin, three new papules developed, one on the central portion of the upper lip and one on each lateral aspect of the chin These papules grew rapidly until they reached a diameter of 2 cm, were verrucous in appearance and exuded a clear serous fluid All laboratory work (including biopsy) was repeated, but results were again negative The patient was evacuated to the United States by plane and admitted to Letterman General Hospital on July 26 Smears, cultures, animal inoculation, biopsy, serologic and blood examinations, urinalysis and roentgenograms of the chest have revealed no abnormalities The lesions continued to spread and have gradually involved the entire chin, lower lip and midportion of the upper lip Three weeks ago the mucosa over the soft palate, uvula, pharynx and tonsillar areas became erythematous, causing some pain on deglutition Topical applications have consisted of boric acid, benzalkonium chloride and penicillin and bichloride of mercury compresses Penicillin in oil (300,000 units) was given intramuscularly daily for ten days Two intravenous injections of oxophenarsine hydrochloride were administered Nitrofurazone was applied to the lesions for twenty-six days None of these medications was of benefit Fractional dosage of low voltage roentgen therapy has seemed to retard further extension of the lesions but has not caused involution

DISCUSSION

DR HARRY E ALDERSON The patient stated that his trouble started in the nose His nostrils are completely occluded Unfortunately, I was not able to examine his palate My former associate, Dr Esteban Reyes, of San Salvadore, has sent me many photographs of cases of rhinoscleroma, some showing extensive vegetation on the outer part of the nose On the external part of the nose there were verrucous growths not ordinarily associated with rhinoscleroma There could

secondary infection in a patient who has a lowered resistance due to the anemia The 6 month pregnancy in this woman is an unusual finding Only 3 cases of pregnancies carried to term in this group of patients have been reported The patients in these cases had had miscarriages some years before The pregnancy in this patient has gone on in a fairly normal manner Pregnancy may be dangerous for her since severe toxemias have occurred in pregnant women with sickle cell anemia, at times leading to a fatal termination

Multiple Benign Cystic Epithelioma Presented by DR EDWARD LEVIN

Syringocystadenoma Presented by DR FREDERICK G NOVY JR

DISCUSSION

DR NELSON PAUL ANDERSON, Los Angeles I appreciate having observed this group of cases I should like to comment on the case presented by Dr Novy as one of syringocystadenoma I think that is undoubtedly the correct diagnosis Many different terms have been applied to this condition Syringocystadenoma, I think, is primarily a benign adenomatous condition, involving the sweat ducts and glands It is fairly common about the lower eyelids and the axillas I do not know why the term "syringoma" is sometimes used Pollitzer's translation of Darier's book has a photograph labeled syringoma, showing involvement of the lower eyelids I do not think that biopsy is ordinarily done when the condition occurs on the lower eyelids

The case presented by Dr Ervin Epstein as one of multiple cutaneous neuromas is the first case of this condition I have ever observed, and I was not able to make a clinical diagnosis I have seen 2 cases, 1 with a solitary nodule and the other with three or four discrete nodules which clinically appeared to be fibromas However, this diagnosis could not be confirmed histologically

There was a report by Wile and Montgomery several years ago of extensive involvement of one of the breasts in a woman As I recall it, pain was a marked clinical feature

DR WERNER W DUEMLING, San Diego The case that interested me most in this group was the rare case of cutaneous neuroma, and I should like to emphasize the word "rare" The case which Dr Anderson credited to Dr Montgomery was the case which I reported in the ARCHIVES in February 1929 The condition, as I remember, was first described by Duhring My case was the fifth reported in the literature Birchoff straightened us out on the histology of this lesion and pointed out that there are two types of cutaneous neuromas, the true and the false The true type, of course, is made up of medullated and nonmedullated bundles of nerve fibers intertwined or interlaced, much as we saw in this section In the false type the fibers arise from neurilemma In the case which I presented the lesion involved one half of the breast area and was dull brownish red in color and extremely sensitive Special stains revealed it to be a true neuroma The patients always complain of pain and hyperesthesia

DR HIRAM E MILLER, San Francisco The patient with cutaneous neuroma without pain is of particular interest to me As far as I can recall, the few patients whom I have seen or have read about have had pain There is a report by Kyrle in Ormsby's textbook (1943) on a similar lesion without pain, described as "unripe" neuroma to account for the absence of pain

A biopsy section studied by Dr Gerson R Biskind revealed neuroma The sections showed a loose fibrous stroma covered on one aspect by a thin layer of skin In the stroma were several sharply demarcated bundles of cellular tissue that had a limiting membrane of fibrous tissue The cells had a slender almost wavy nucleus The stroma around the cells was pink and homogeneous but in places might be fibrillar The cells did not show distinct palisading with the formation of characteristic Verocay bodies, this process, however, was suggested in many places The over-all pattern was highly suggestive of an amputation neuroma, except that the bundles were much more cellular The site of excision should be observed for possible recurrence The present histologic structure showed no evidence of malignancy

DISCUSSION

DR HIRAM E MILLER I am not familiar with neuromas that are not painful In my patients, all of them were painful Kyrle, however (quoted in the textbook by Ormsby and Montgomery), described painless tumors in the retroauricular region in a patient who had neuromas for three years They were lentil-sized, translucent areas Histologically the lesions consisted of bundles of delicate nerve fibers He stated that pain was absent because they were "unripe" neuromas The lesions in this case may be of a similar nature

DR ERVIN EPSTEIN This disease is apparently rare It usually follows trauma The lesions seem to resemble amputation neuromas histologically They are usually painful, but some do exist for long periods before pain develops According to the literature, all become painful eventually Plastic surgery followed by skin graft would seem to be the treatment of choice in this case

Lichen Sclerosus et Atrophicans, Inframammary, Inguinal and Vulvar Presented by DR ERVIN EPSTEIN

Lupus Erythematosus Presented by DR NORMAN N EPSTEIN

Calcinosis Cutis (Circumscribed Form) Presented by DR HIRAM E MILLER

A Case for Diagnosis (Actinic Dermatitis? Lupus Erythematosus?) Presented by DR REES B REES

A Case for Diagnosis (Actinic Dermatitis?) Presented by DR FRANCES A TORREY

Bowen's Disease? Presented by DR GRANT MORROW

Scleroderma (Localized) Presented by DR ROBERT A STEWART

Nevoxanthoma-Endothelioma Presented by DR MAX KRAUSE

A Case for Diagnosis (Scaly Erythroderma? Lymphoblastoma?) Presented by DR EDWARD A LEVIN

Thymoma Presented by DR FRANCES A TORREY

The case of J N S, a 36 year old white woman, was previously presented before the San Francisco Dermatological Society on April 26 and Sept 13, 1946

Since the last presentation the following roentgen therapy was given From Sept 16 to Oct 3, 1946, a total dose of 3,000 r was delivered to each of two fields, the right and left axilla, with a filtration of 0 25 mm of copper and 1 mm of aluminum From Nov 19 to Nov 27, 1946, an area measuring 2 5 by 6 cm in the anterior cervical region was given 2,400 r with a filtration of 0 25 mm of copper and 1 mm of aluminum From Jan 20 to Feb 11, 1947, an area in the left cervical region measuring 7 by 7 cm received 3,000 r with a filtration of 0 25 mm of copper and 1 mm of aluminum



Thymoma in J N S

A Case for Diagnosis Multiple Benign Pigmented Fibroma Presented by DR ARNE E INGELS

D D, a white married woman aged 48, had had a lesion on her heel which started at the age of 15, a lump on the dorsum of the foot and one on the right forearm There was a gradual increase in the size of the tumor of the Achilles tendon, until it was 4 to 5 cm in diameter by June 29, 1945 The two other lesions increased slowly in size They have been brownish-blackish in appearance all the time The tumor on the dorsum of the foot was flat, blackish-brownish and approximately 1 5 cm in diameter

The larger ones appeared to be made up of conglomerate masses of smaller ones They were, for the most part, a normal cutaneous color Some were slightly paler They seemed nontender and showed none of the signs of an inflammatory process

Since birth the lesions appear to be slowly disappearing Many of the smaller ones seem to have disappeared The largest ones are on the scalp, and several of these are a faint xanthomatous yellow, which was not so notable earlier When I last saw the baby I thought I could feel an enlarged firm nontender spleen This was not confirmed by a pediatrician who subsequently examined her

A biopsy, Aug 7, 1946, was reported by the pathologist to show stratified squamous epithelium with normal subcuticular structures In one margin of the section the subepithelial tissue was infiltrated by monocytic series cells consisting of lymphocytes and plasma cells This process extended into the deepest layers of the skin and was a diffuse rather than a dense pattern

The Kahn and Wassermann reactions were negative at birth The Kahn and Kline reactions were again negative on November 9 The cholesterol content of the blood was 150 mg per hundred cubic centimeters on November 9 The hemogram and the differential count were essentially normal

DISCUSSION

DR MERLIN T-R MAYNARD (San Jose) Is there any history of bromide ingestion in the mother?

DR H V ALLINGTON I did not question her about that

DR REES B REES I think that the occasional tremendous activity of the sebaceous glands in young children is of interest It is observed in clinics in normal babies, and babies go through that period without much difficulty

DR H V ALLINGTON I did not get the impression that the sebaceous glandular apparatus was involved I considered the possibility of its being a lymphoblastoma Also, because of the yellowish color in several of the scalp lesions at the present time, I wonder about this being another case of nevoxanthoendothelioma It is possible that if a biopsy specimen were to be taken from one of the scalp lesions at the present time, it would show a more characteristic picture

JOINT MEETING OF THE SAN FRANCISCO, LOS ANGELES AND PACIFIC NORTHWEST DERMATOLOGICAL SOCIETIES

Ervin Epstein, M D, *Presiding*

Jan 18, 1947

A Case for Diagnosis Pemphigus Vegetans? Presented by LIEUT COL ROBERT S HIGDON, Letterman General Hospital, San Francisco (by invitation)

Lupus Erythematosus or Dermatomyositis? Presented by DR EDWARD LEVIN

DISCUSSION

DR ERNEST K STRATTON, San Francisco, Calif Since reporting in 1942 the experimental transfer to mice from a patient with mycosis fungoides, I have made similar transfers of tissues from 3 additional patients

The first was transferred on March 26, 1945 The case was far advanced at the time, and the patient died shortly thereafter All the animal inoculations have been negative to date The second, from 1 of the patients shown here this morning, was transferred on May 29, 1945 The specimen was placed in an icebox at —78 C for seven days It was then thawed and emulsified, and portions were injected into the brains of 6 mice and into the peritoneal cavity of another 6 One of these mice (brain injected) died on June 10, 1946 (thirteen months after injection) Its liver was enlarged five times and its spleen enlarged twenty times Microscopic studies showed infiltrations similar to the picture of mycosis fungoides

The third transfer, from M J, was made on July 31, 1945 The tissue was first emulsified and then passed through a Seitz filter before being injected into 6 mice intraperitoneally On May 6, 1946 (ten months after injection) 1 of the mice became ill and was killed Its spleen was ten times normal size Microscopically it showed a mycosis fungoides type of cellular infiltration A portion of this spleen was emulsified, and a second passage has been made

On July 31, 1945, when the first passage was made, whole blood from this patient was also injected intraperitoneally into 6 mice These mice were killed recently and their organs were normal The original emulsion from this patient was also inoculated onto the chorioallantoic membranes of eggs In 1 embryo tumors developed on the eye and on the heart This type of reaction is being studied further

Another interesting observation in the last 2 cases was the fact that the mouse tumors were produced by using a "cell-free" emulsion (in the case in which the tissue was Seitz filtered before injection) and a "dead cell" emulsion (in the case in which the tissue was frozen for seven days before injection)

In view of these findings, it would seem that if there could be any correlation between mycosis fungoides in the human being and that reaction which has been observed in the mouse (in 3 cases out of 4), it would, I believe, favor the theory that the etiologic agent in mycosis fungoides is a toxin or a virus rather than a malignant tumor cell

DR D E H CLEVELAND, Vancouver, B C The most interesting point about these cases of mycosis fungoides is the fact that the patients have had the disease for a length of time and yet are in excellent general health Also, only 1 of them, I believe, had had anything resembling the ulcerative lesions of mycosis fungoides, squashed-tomato-like tumors I also belong to that group who regard mycosis fungoides as a clinical and not a histopathologic diagnosis Udo Wile put it in those words almost—mycosis fungoides is a clinical and not a pathologic entity Beerman says that any case shown to be a manifestation of Hodgkin's or lymphosarcoma should be so named (*Am J M Sc* **211**:479, 1946) The histopathologic characteristics are seen from time to time in other groups of lymphoblastomas Recently an autopsy on a patient whom I had had under observation with clinical mycosis fungoides for about two to three years showed the disease to be unquestionably giant follicular lymphoblastoma Antemortem biopsy of a lymph node showed the same Ulcerative lesions gradually developed

I have been studying our cases of malignant lymphoma in the Vancouver General Hospital for a ten year period Approximately 50 per cent of the patients with Hodgkin's disease and 50 per cent of those with follicular lymphoma (giant follicular lymphoblastoma) had generalized erythroderma exfoliativa, in many ulcerated In 1938 Dr Ormsby said, when observing 1 of these cases, "If I had

cm The sections revealed a young-appearing mesenchymal connective tissue and surrounding fat, both containing numerous endothelium-lined vessels and a mild inflammatory reaction There were several focal areas of necrotic degeneration with surrounding pseudopalisading of cells There were also bits of eosinophilic intercellular material suggesting the presence of fibrosis The diagnosis was "subcutaneous nodule consistent with rheumatic nodule or with granuloma annulare"

No treatment was given

Erythema Annulare Centrifugum Presented by DR ERVIN EPSTEIN

Sickle Cell Anemia with Ulcers on the Legs Presented by DR NORMAN N EPSTEIN

DISCUSSION

DR HIRAM E MILLER, San Francisco My case is presented as an example of subcutaneous granuloma annulare This is the second patient that we have seen with this condition in the past year The lesions in both cases were firm, subcutaneous, nontender and cherry sized and were tightly bound down to the deeper structures The focal areas of coagulation necrosis with a palisade-like arrangement of the infiltrate seem to be compatible with the diagnosis Grauer and Wile described this variant of granuloma annulare in the ARCHIVES (**30** 785, 1934)

DR ERVIN EPSTEIN, San Francisco In the patient with erythema annulare centrifugum the lesions change a great deal from week to week I have been seeing her for more than a year, so I can make this statement with certainty The condition appeared entirely different one week ago At one time it was thought that the condition might be granuloma annulare, but further observation has established the present diagnosis This histologic picture is consistent with erythema annulare centrifugum At first the possibility of a phenolphthalein eruption was also considered, but the discontinuance of the use of this drug for the past year has not resulted in a lessening of the activity of the condition The patient has had a great deal of treatment, with little benefit However, sulfadiazine by mouth has repeatedly resulted in prompt clearing of the eruption Discontinuance of administration results in just as prompt recurrences

DR NORMAN N EPSTEIN, San Francisco In our experience sickle cell anemia is rare The subject was well covered by Cummer and La Rocco in 1940 Certain interesting points relating to this condition might be mentioned The name "sicklemia" probably fits the condition much better because people with sickling of their red blood cells are not always anemic Many of them go into periods of profound anemia, and later their blood may regenerate to a normal condition The anemia may be transient in this group of patients It is a condition primarily found in Negroes but is not absolutely restricted to that race Some cases have been reported in the white race, among Sicilians and Mexicans About 8 per cent of Negroes have sickling of their blood I do not know in what percentage anemia develops The anemia found is of the hemolytic type Ulcers are one of the symptoms Other symptoms may be referable to the liver, heart, spleen and other viscera The origin of the ulcers is well understood They are peculiarly shaped It is not a specific ulceration as far as one can determine Whether it is due to the anemia is a question Certainly, in other severe anemias ulcers of the legs are not reported frequently But in 75 per cent of the patients with sickle cell anemia these ulcers do occur They are probably due to trauma plus

given Apparently the antireticular cytotoxic serum stimulates the reticuloendothelial tissue

DR W H GOECKERMAN, Hollywood, Calif Regarding the case presented by Dr Keddie, I cannot tell you what the name of the condition is, but certainly it is not papulonecrotic tuberculid This patient has none of the characteristics of Hodgkin's disease of the skin We must allow for other possibilities In this young man the process has been present for years and years, and yet it disappears when exposed to the sun rays systematically What it is, I do not know It seems to me an interesting picture, but I am sure it is not papulonecrotic tuberculid The papulonecrotic tuberculids have a characteristic picture I have seen a great many of them

DR GRANT MORROW, San Francisco I should like to comment on the case of Dr Ingels' (multiple benign pigmented fibroma) I think it is benign melanoma We had 2 patients recently in whom lesions developed on the dorsum of the feet Both showed melanoma of benign variety

DR FRANCES A TORREY, San Francisco Concerning the case of malignant thymoma that I presented, the diagnosis was made only after examination of several biopsies I understand that thymomas are rare, and Douglas Symners (Malignant Tumors and Tumor-Like Growths, Ann Surg **95** 544, 1932) reported 25 malignant tumors or tumor-like growth of the thymic area in 17,000 autopsies (0 14 per cent) from the Pathology Laboratory of the Bellevue Hospital Hamberger (*Arch Path* **36** 37, 1943) reported that in 6,000 autopsies there were found 41 instances of tumors or enlargement of the thymus Of these only 3 were found to be malignant Under the classification of thymoma five types of malignant growths may occur (1) perithelioma from connective tissue of the walls of the blood vessels, (2) lymphosarcoma from the lymphocytic elements, (3) epithelioma from the epithelial reticulum cells, (4) spindle cell sarcoma from the connective tissue framework and (5) Hodgkin's disease from lymphocytes in the thymus Of these five, lymphosarcoma and Hodgkin's disease are the most radiosensitive This tumor was considered to be of the Hodgkin type after the first biopsy was made, and it was treated accordingly The tumor did not show any regression until after the diagnosis of epithelioma was made and the large dosage of roentgen rays was given Although the regression of the tumor has been remarkable, the prognosis, of course, is extremely poor There was a large, widely infiltrating lesion of the mediastinum that spread by direct extension to the axillas It is amazing that there has been no sign of metastasis, only the spread by direct extension

DR ARNE E INGELS, San Francisco My case was presented with the idea of clarifying the diagnosis For the pathologic diagnosis increased vascularity only does not satisfy, obviously I even thought the condition resembled pseudoxanthoma elasticum histopathologically The predominant feature was a great increase in elastic tissue, even clumping and homogenization However, clinically it did not correspond to this Otherwise, it might be a more benign xanthoma The tumor was treated with roentgen rays years ago and lost the picture of unusual singular blackish melanotic pigmentation The remaining tumor on the dorsum of the foot still retains the pigment Microscopically, it shows basal cell melanin changes within the normal So, what can it be but a benign tumor of elastic origin?

DR FRANCES M KEDDIE, San Francisco The condition of the student may not be Hodgkin's disease Clinically it does not fit with the histologic examination I had a note from Dr Hamilton Montgomery, who said it looked like malignant lymphoma The description was made by Dr Bostick, who has been interested in Hodgkin's disease for a long time I met Dr Bostick in the hall just now, and he told me he feels fairly certain it is Hodgkin's disease

DR ERVIN EPSTEIN, Oakland, Calif The interesting feature in the case of multiple neuroma, of course, is the rarity of this condition In reviewing the literature, one is impressed by the repeated history of trauma preceding the lesions The patient refused to allow surgical intervention, so roentgen therapy is being attempted Despite the fact that nerve tissue is considered to be relatively insensitive to radiation, even one treatment of 200 r produced some improvement

Circumscribed Myxedema of the Legs Presented by DR STUART C WAY and DR JAMES R DRAKE

A Case for Diagnosis Nevoxanthoendothelioma? Presented by DR H V ALLINGTON (From the Berkeley Hospital Clinic, Berkeley, Calif)

The case of G M C, a 6 month old Negro baby girl, was presented on Nov 15, 1946, at the meeting of the San Francisco Dermatological Society

Nevoxanthoendothelioma Presented by DR MAX E KRAUSE

The case of G T, a white boy aged 9 months, was presented at the meeting of the San Francisco Dermatological Society on Nov 15, 1946 Thus far there have been no signs of regression of the lesions

Necrobiosis Lipoidica Diabeticorum Presented by DR FRANCES M KEDDIE

DISCUSSION

DR NELSON PAUL ANDERSON, Los Angeles Localized myxedema may come on acutely and be so inflammatory as to mislead the thyroid surgeon and the cardiologist I have seen one instance of localized myxedema in a Chinese leper who had undergone thyroidectomy In a recent article, someone writing on the subject of leprosy described lesions of this type occurring in connection with it

Necrobiosis lipoidica diabeticorum was first described as a clinical entity in the latter part of the third decade of this century I should like to call your attention to an article in the *American Journal of Medical Sciences* (Goldstein, E, and Harri, J Xanthoma Diabeticorum An Unusual Process of Evolution, *Am J M Sc* 173-195 [Feb] 1927)

DR MERLIN TREVOR-ROPER MAYNARD, San Jose, Calif For the Negro child with the diagnosis of nevoxanthoendothelioma I should like to offer the diagnosis of urticaria pigmentosum In this child wheals would definitely be produced after stroking I think that a biopsy and stains for mast cells should be made, which are characteristic of this condition

DR J WALTER WILSON, Los Angeles I too should like to follow Dr Maynard's suggestion as to the diagnosis in the case which Dr Allington presented under the title of "nevoxanthoendothelioma" I think that the correct diagnosis is urticaria pigmentosa I was interested in the conversation with the mother, who states that whenever the child is rubbed, wheals appear in "little spots" I tried to elicit the sign known as "Darier's sign," in which friction produces whealing limited to the pigmented areas I do not believe that this can be demonstrated

DR H V ALLINGTON, Oakland, Calif This is the third patient whom I have recently seen with the complaint of dryness of the mucous membranes of the eyes, nose and mouth This problem has been discussed in the American literature by ophthalmologists more than by dermatologists (MacLean, A L Sjogren Syndrome, *Bull Johns Hopkins Hosp* **76** 179-191 [May] 1945, Freedman, B, and Gerrard, H Sjogren's Syndrome Treated with Stilbestrol, *California and West Med* **64** 31 [Jan] 1946), deRoetth, A Hypofunction of the Lacrimal Gland and the Sjogren's Syndrome, *Lancet* **65** 423-425 [Dec] 1945) It has been reported as occurring in women after the menopause It has usually been associated with other diseases, especially arthritis or focal infection In some patients there has been a swelling of the salivary and lacrimal glands early in the course of the disease, with atrophy later The changes in the eyes may be marked, sometimes progressing to a severe keratitis and corneal erosions

Vitamin A deficiency has been suspected, and administration of vitamin A has been reported as helping in some cases It made no difference in this patient and in 1 other whom I have seen

Because of its association with the menopause, an endocrine background has been suspected, and the administration of stilbestrol has been reported as helping temporarily

Scleroderma Circumscriptum and Morphea Guttata Presented by DR CHARLES W MCNITT, Reno, Nev

Localized Scleroderma Presented by DR FRANCES A TORREY

Scleroderma? Diabetes Mellitus Syphilis of the Central Nervous System? Presented by DR JULIAN C LUNSFORD, Oakland, Calif

Scleroderma Presented by DR DAVID BOHR (by invitation)

Scleroderma Presented by DR DAVID BOHR (by invitation)

Poikiloscleroderma with Calcinosis Presented by DR FRANCES A TORREY

Calcinosis Cutis Presented by DR HIRAM E MILLER

DISCUSSION

DR WALTER R NICKEL, San Diego, Calif The case of a single lesion on the back (localized scleroderma, presented by Dr Torrey) I think is a case of lichen sclerosis et atrophicus There is definite plugging in the central portion of the lesion The condition of the man with stiffness of his hands and forearms I would say resembles more closely acrosclerosis There is typical sclerosis of the "V" of the neck area, along with inability to open his mouth fully or produce wrinkling of the forehead

DR D E H CLEVELAND, Vancouver, B C Are there any further suggestions as to treatment? In 1 case of acrosclerosis and scleroderma I have used 150,000 units of calciferol (vitamin D_2) daily The patient thinks he is better, but I do not think he is

DR NELSON PAUL ANDERSON, Los Angeles Etamon chloride® (tetraethyl ammonium chloride), a new drug produced by Parke, Davis and Company, is being used at the University of Michigan for peripheral vascular disorders It is

On the lower portion of the Achilles tendon there is a discolored, firm, sessile lesion, 3 cm in diameter, which is grayish-brownish pink It is freely movable and has no infiltrating growth The dorsum of the right foot shows a brownish black, slightly raised lesion, 1 5 cm in diameter, which is well defined and freely movable with no inflammatory changes On the right forearm is a scar from the excision of one of the lesions There is no glandular enlargement

The physical examination shows a healthy woman with abdominal scar formations from previous operations for cystic ovaries, appendicitis and peritonitis The scalp shows four atheromas On the left side of her face is a darkly pigmented mole

The Wassermann reactions were negative on repeated examinations The blood count showed 4,100,000 red cells, 79 2 per cent hemoglobin, 6,400 leukocytes, 78 per cent polymorphonuclear neutrophils, 18 per cent lymphocytes, 1 per cent eosinophils

Hodgkin's Disease of the Skin (Generalized Erythroderma with Scattered Papules) Presented by DR FRANCES M KEDDIE

A Case for Diagnosis Hodgkin's Disease of the Skin Presented by DR FRANCES M KEDDIE

G E, a 17 year old student, has had a papular eruption since he was 7 years old This eruption has recurred each winter and has cleared up each summer after about two weeks of exposure to the sun With each recurrence there have been more lesions which have gradually become larger in size

The eruption is polymorphous There are papules and firm pustules 1 to 2 cm in diameter These are in the skin and can be freely moved over the underlying tissue They heal with slight scarring Some are excoriated, but few cause itching The lesions are distributed on the trunk and on the extremities

The physical examination showed a normal healthy boy except for the cutaneous disorder The blood count and urinalysis gave normal results

Biopsy has been twice performed, and on each examination the histopathologic process was essentially the same (One section was made at the Mayo Clinic in May 1944 and the second at the University of California in December 1946) The second section is reported on by Dr Bostick as follows "Immediately beneath the epithelium and in the subpapillary dermis there was a proliferative reaction composed of large pleomorphic cells, often in the giant form and some of them with prominent nucleoli There was a background of round cells, scattered fibroblasts, granular leukocytes and eosinophils The most proliferating and pleomorphic cells seemed to be of reticuloendothelial origin, and these extended in small groups down to the underlying dermis Careful examination with acid-fast stains, Giemsa stains and Gram stains showed no evidence of specific organisms"

A diagnosis of Habermann's disease was made in 1944, and the treatment that was given included administration of sulfonamide compounds, ultraviolet radiation and vitamins A and D in large doses None of these caused abatement of the eruption No roentgen therapy has been given

Mycosis Fungoides, Plaque Type Presented by DR FRANCES A TORREY

Mycosis Fungoides Pruritic Infiltrated Patches Presented by DR FRANCES A TORREY

The types presented today run the gamut of scleroderma types, except for the "cardboard" form Scleroderma circumscriptum may be found with a widespread or general distribution and should not be classed as "localized" Also, diffuse scleroderma requires a better term than generalized scleroderma, as it is often confined to places such as the hands, forearms, feet and legs or face and neck The use of "white spot disease" has largely been given up, because it led to confusion between lichen sclerosis et atrophicus and morphea

The woman of 27 years of age (presented by Dr McNitt) in whom there was a relatively gradual onset of scleroderma is interesting because of the possibility of an etiologic endocrine factor associated with her pregnancy The condition is largely limited to one side She was found to have apical abscess of the second molar and an impacted wisdom tooth They should be cared for These patients often improve greatly after focal infection has been removed She has had no history of exposure to arsenic While the condition originally progressed steadily, with greater and greater spread of the lesions, she has improved on the following medication thyroid extract, 3 grains (0 2 Gm) daily, 150,000 units of vitamin A and a pancreatic extract in the form of padutin ©

To my mind this case is definitely one of scleroderma and morphea guttata Histologically, the atrophic epithelium and the hypertrophic collagen bundles characteristic of scleroderma are present The picture of lichen sclerosis et atrophicus is not present

DR HIRAM E MILLER, San Francisco I think it should be pointed out that in the case presented by Dr Bohr (S W) sympathectomy was done without any benefit I should like to state also that the large biopsy scar was the result of the surgical removal of a large piece of tissue for chemical studies

In the case presented by Dr Torrey as one of poikiloscleroderma with calcinosis there is no doubt about the diagnosis It was presented here at the last meeting in 1939

In my patient, unfortunately, all the lesions were excised except one on the left knee In both instances calcinosis cutis was of circumscribed variety

Ervin Epstein, M D , *President*

Frances M Keddie, M D , *Secretary-Treasurer*

March 21, 1947

Recalcitrant Pustular Acrodermatitis of the Hands Presented by DR J M READ (by invitation, for DR OTTO E L SCHMIDT)

Erythema Perstans Presented by DR HARRY J TEMPLETON

Hansen's Disease Presented by DR J M READ (by invitation, for DR OTTO E L SCHMIDT)

Basal Cell Epithelioma, Morphea-Like Sclerosing Type in the Nasolabial Fold Presented by DR FRANCES A TORREY

Lichen Sclerosus et Atrophicus of the Female Breast Presented by DR ARNE E INGELS

not seen the slides, I would have called it mycosis fungoides" Jackson would have called it Hodgkin's granuloma Extensive cutaneous involvement does not present the picture as generally seen—great big lymph nodes in the neck The big nodes are chiefly in the axillas and groins

DR NELSON PAUL ANDERSON, Los Angeles I cannot agree with the diagnosis presented by Dr Ingels I believe that these lesions are really fibroxanthomas in which fat stains will undoubtedly show definite fat globules These give that peculiar yellowish color to the lesions, which was well shown in the one over the Achilles tendon You will not find xanthoma cells because the fibrotic tissue is predominant I do not think that they are ordinary pigmented fibromas

One patient with mycosis fungoides showed poikiloderma-like cutaneous changes on the anterior aspect of the trunk

Finally, I should like to call your attention to the more recent work dealing with mycosis fungoides and Hodgkin's disease More particularly, as dermatologists, we are interested in mycosis fungoides treated with nitrogen mustard Earl Osborne, of Buffalo, personally told of 3 cases of mycosis fungoides responding well to nitrogen mustard treatment Four cases at the Cedars of Lebanon Hospital in Los Angeles have responded with apparent involution of the tumors Two more patients are about to be treated, and 1 additional patient at the General Hospital is now being treated with nitrogen mustard Dr Ray Allington, who is acquainted with the cases at the County Hospital, might tell us of his experience with nitrogen mustard.

DR RAY ALLINGTON, Los Angeles I do not know the exact dosage recommended, but I believe it is given in small amounts in isotonic sodium chloride solution by means of intravenous drip and is given only three or four times on consecutive days to complete a single series One of the patients in our ward has had such a series of one of the nitrogen mustard preparations and has responded amazingly well Two of his lesions had been given roentgen therapy, but all were benefited by the drug We should like to see more patients so treated

DR FLETCHER HALL, Los Angeles Discussants so far have taken up all the cases in the group, except the case of Hodgkin's disease of the skin (?) presented by Dr Keddie, which I should like to introduce into the discussion I could not help but think of the diagnosis of papulonecrotic tuberculid when I first saw the patient Then, on reading in the history sheet what the Mayo Clinic said, I was thrown off the track I could not see any microscopic signs in the slide exhibited which would account for the clinical appearance of the lesions, and I wonder if it was a truly representative section of one of the lesions as presented by the patient today In view of the history and clinical findings, I should treat this patient for papulonecrotic tuberculid

DR SAMUEL AYRES JR, Los Angeles I felt the same way about this case The distribution of the lesions on the legs and arms predominates, and the eruption is worse during the cold weather It is better in the summer It strikes me that papulonecrotic tuberculid is the most probable diagnosis

In regard to the cases of mycosis fungoides I should like to say that I have been working with the A C S (antireticular cytotoxic serum) during the last year or so I have 1 patient who apparently has had a remission with the serum which was furnished by Dr Straus, of the Cedars of Lebanon Hospital The case was typical, microscopically and clinically, although not a far advanced one One case in which the serum failed was a far advanced case Another case apparently got out of control A C S serum, I think, is worthy of a trial, with little risk The results are not as dramatic as those reported with nitrogen mustard Dr Straus, pathologist at the Cedars of Lebanon Hospital, told me personally of a patient with lymphosarcoma who apparently recovered after A C S was

areas of erythema on the trunk and proximal portions of the extremities and puffiness of the face and ankles Muscle biopsy showed mild dermatitis and myositis

I want particularly to get suggestions as to treatment The patient has had reactions to drugs in the past I thought that the condition was fairly closely related to scleroderma and gave her an insulin-free pancreatic extract, but her condition is unchanged

DR ERVIN EPSTEIN In 1 case of dermatomyositis I have gone through the gamut of therapeutic possibilities I have given adrenal cortical extract, penicillin, an insulin-free pancreatic tissue extract, glycine and ephedrine Now the patient is getting fever therapy The disease does not seem to be improving

DR GEORGE V KULCHAR As I recall, particularly in 1 case, pyrotherapy was the most effective form of treatment

DR FREDERICK G NOVY JR My impression is that the cutaneous changes fit in better with the diagnosis of dermatomyositis than of periarteritis nodosa

Acne Rosacea with Ocular Involvement Presented by DR J M READ (by invitation, for DR OTTO E L SCHMIDT)

A B, a 46 year old married white American woman, was first seen on March 17, 1945, because of a rash on her face of six to eight weeks' duration which has appeared in the spring and fall for the past eight to nine years For two weeks she has noted photophobia and redness of her eyes The photophobia has appeared every year in spring and fall, at the same time as the rash on the face She gave no history of atopy

The erythematous patches and the acneform pustules are confined to the central oval of her face The keratoconjunctivitis is more pronounced in her left eye Treatment has consisted of sulfur-resorcin lotion and riboflavin, 10 mg three times daily

DISCUSSION

DR HARRY J TEMPLETON This process is rather typical of rosacea keratitis, which has been described by ophthalmologists as yielding specifically to riboflavin therapy

DR HARRY E ALDERSON Naturally one would think of the possibility of achlorhydria It is seen fairly often in rosacea with acne and in the keratitis rosacea which this patient presents

DR REES B REES The ophthalmologists think that superficial fractionated roentgen therapy is of real value in this condition Perhaps 50 r, unfiltered, once a week for several weeks, might be beneficial

DR MERLIN T-R MAYNARD (San Jose) Along the line of therapy, one seems always to have trouble in getting a response I have a patient, a boy of 14 years of age, whose mother has had severe rosacea for many years This boy had grown to be 6 feet 4 inches (193 cm) tall When I saw him he had severe rosacea with large acne pustules and keratitis such as this woman has I gave him vitamin A, 100,000 to 150,000 units, 15 mg of riboflavin by mouth daily and 5 mg of riboflavin by injection every third day Within ninety days he was free of all symptoms, including the keratitis I think that this woman should be given active therapy along these lines

A Case for Diagnosis Unusual Fragility of the Skin (Related to Epidermolysis Bullosa or Ehlers-Danlos Syndrome) Presented by DR HARRY J TEMPLETON, Oakland, Calif

Epidermolysis Bullosa Presented by DR NORMAN N EPSTEIN

Sjogren's Syndrome Presented by DR H V ALLINGTON, Oakland, Calif

A G, a white woman aged 63 years, has had dryness of the mucous membranes of her mouth and eyes since 1934 This has become so severe that she has to wet her mouth with water to enable her to talk Her eyes are so dry and sticky in the morning that she has to wash them with water to get them open There are also periods when she appears to have an excess of a sticky and tenacious mucus in her mouth Her symptoms started at about the time of her menopause She has had the usual diseases and also had erysipelas and pneumonia when she was a child In 1927 she had a "nervous breakdown," which was thought to be from overwork Severe attacks of arthritis began about 1937, and she has had recurrences since then lasting from three to four days but apparently decreasing in severity as time goes on A systolic blood pressure of from 170 to 200 mm of mercury has been present for years

There are no objective changes in the mucous membranes The lacrimal glands are not palpable The salivary glands are small but palpable and are not tender

There is clubbing of the finger nails and mild hypertrophic changes in the small joints of her fingers The blood pressure was 200 systolic and 100 diastolic The reaction to the Schirmer test was 7 mm in 5 minutes (normal 21 to 25 mm) Her eyes otherwise were reported normal by Dr J R Sharpsteen, Oakland, Calif, except for a mild defect of conversion The blood count and urinalysis were essentially normal

A vitamin A concentrate of 25,000 units, given three times daily, has been of no benefit Hormones have not yet been tried

DISCUSSION

DR W H GOECKERMAN, Hollywood, Calif The last case interests me more than anything I have observed in years but not because it was called "Sjogren's syndrome," since I do not know whether that means anything If the patient came into my office and told me of the dryness of her mucous membrane, I would not know how to approach the case I went further into the history and talked at some length to the patient She told me that she does not know if she has any coldness in her fingers Her friends have told her that her hands are cold I saw that she had a peculiar sort of erythematous livid condition of her fingers There is a definite vasomotor disturbance, secondary disturbance of nutrition to the finger nails My first thought would be to give her estrogen I think it is not uncommon to see vasomotor disturbance in those along in years, even up into the seventies, as the result of endocrine imbalance I should like to suggest that a systematic effort be made to give estrogen therapy in this case under whatever name you may call it This is to me a mild disturbance which we frequently see for years following the menopause

DR SAMUEL AYRES JR, Los Angeles Perhaps there is some disturbance in the involuntary nervous system Pilocarpine, 1/20 to 1/10 grain (3 to 6 mg) three times daily, might affect the stimulation of the salivary glands and perhaps will stimulate the production of tears

the back of his neck For two months he has had in the joints of his extremities a pain associated with coldness, weakness, swelling and hardening of the skin of his hands and feet In the past two months he has lost 20 pounds (9 Kg)

Examination shows the skin of the face, hands and feet to be hardened and edematous without pitting His hands and feet are cold, but the arterial pulses of both are good There is limitation of movement of about 20 per cent of the hands and feet

The Kahn reaction was negative The electrocardiogram showed a left axis deviation The blood cholesterol was 256 mg per hundred cubic centimeters, sugar 82 mg, urea nitrogen 8 mg, uric acid 4 mg and calcium 9 5 mg Repeated blood cell counts were within normal limits except on one occasion when the eosinophil count was 35 per cent. The roentgenograms of the chest, spine and pelvis showed no abnormalities Examination of the feces did not show blood and parasites

A stellate ganglion block was performed but effected no change Since Sept 3, 1947, seven injections of a pancreatic preparation (padutin®), each of 10 units, have made little difference

DISCUSSION

DR ARNE E INGELS The combination of padutin® with thyroid should be considered

DR EUGENE OSTWALD There is a difference between oral and muscular administration of padutin® I believe that the intramuscular administration is by far better and more effective Intramuscular injections can be given without any ill effect, and without reaction, once or twice daily for a long period of time

Papulonecrotic Tuberculid or Lupus Erythematosus? Presented by DR RICHARD O PFAFF, San Jose, Calif

Unexplained Edema of Nose Presented by DR FREDERICK G NOVY JR

Poikiloderma Vasculare Atrophicans (Jacobi) Presented by DR GRANT MORROW

R S, a white woman aged 54, born in Austria of Italian parentage, was first seen on June 9, 1947 She stated that itching of her arms and legs started six months ago and has gradually increased in severity On the skin of the arms and legs are symmetric, round, atrophic, 1 to 3 cm areas with telangiectasis The skin is dry and scaly The dermatitis simulates that of roentgen dermatitis

Physical examination showed the blood pressure to be 140 systolic and 80 diastolic There were no abnormal findings The blood cell count was within normal limits The Rumpel-Leede test showed increased capillary fragility The treatment has consisted of rutin (vitamin P), 60 mg three times a day The pruritus has greatly decreased The Rumpel-Leede reaction is now only slightly positive, and the patient feels much improved

DISCUSSION

DR EUGENE OSTWALD I would like to call this acrodermatitis chronica atrophicans, and I believe that the patient presents rather characteristic changes The skin at the elbows is bluish red, wrinkled and parchment like

supplied for experimental use only At the University of Michigan they have used it in this group of peripheral vascular diseases, including Berger's disease In 1 personal case of Raynaud's syndrome with scleroderma-like changes in the skin, together with definite ulceration and impending gangrene, I felt that amputation would be required shortly The patient improved after therapy with this new drug, and the affected digits apparently have been saved Persons so treated should not drive a car for several hours as there is prompt interference with visual accommodation While I do not feel that this drug by any means solves the problem of peripheral vascular disease, yet it is to be considered for use in persons who have ulceration, impending ulceration or early gangrene of digits

Dr Norman N Epstein, San Francisco In the case of generalized scleroderma (presented by Dr Bohr) the condition was severe when the patient first came into the clinic It was so severe that he could hardly open his mouth He was given artificial fever therapy With this, he improved A second patient came in at the same time with a condition which was almost identical and was also given fever therapy This woman did not improve We have not tried fever therapy in many cases, but I think it has benefited that man Certainly, it increased the basal metabolism and increased the blood flow to the skin I think it is worth while to try the artificial fever therapy, once a week for ten weeks, in cases of this type

Dr Franklin I Ball, Hollywood, Calif With regard to the diagnosis of scleroderma in a patient who is diabetic (case presented by Dr Lunsford), if this is an instance of scleroderma, it is certainly not the usual picture which one expects to see I was much more impressed with the possibility that this was an instance of degeneration of the connective tissue elements of the skin, possibly amyloidosis cutis

Dr W H Goeckerman, Hollywood, Calif I am interested in that woman whose lesions were essentially unilateral (case presented by Dr McNitt) I would suggest the diagnosis of lichen albus For years there has been discussion as to whether lichen albus belongs to the lichen planus group We got away from that conception, but where it does belong I do not know I still hold that lichen albus is a disease entity, not of the same nature as any form of scleroderma or of lichen sclerosis et atrophicus The cause is entirely obscure

Dr Walter R Nickel, San Diego, Calif There is no evidence of lichen sclerosis et atrophicus in the girl The upper layer of the corium showed typical sclerosis, with atrophy of the appendages, without the homogenized edematous character of lichen sclerosis I think it is a pure case of unilateral scleroderma

Dr Rees B Rees, San Francisco I agree with the last speaker

Dr Charles W McNitt, Reno, Nev I believe this interesting group might well form a small symposium on so-called scleroderma I should like to invite you away from the use of that term entirely There will come a time when we will all agree with the conclusions made by Goetz in the "1945 Year Book of Dermatology and Syphilology" that this type should be called multiple progressive systemic sclerosis He does not think that we should call it scleroderma Other interested workers bore out the vascular factor and called it angiitis Some day we may say that Raynaud's disease and dermatomyositis belong in the same group I am willing to admit my ignorance, but I think we should take that broad view In 1928 Allen, in the Archives, described the same morbidity, edema, cellular infiltration, fibrosis and subcutaneous atrophy in the skin in scleroderma, in dermatomyositis scleroderma and in dermatomyositis, and stated that in all there are the same prodromal symptoms, frequent history of rheumatism, rheumatic fever and other evidences of focal infection, which relates them closely

Before examination the patient had received treatment, including roentgen and penicillin therapy According to the patient these did not improve the condition Since then he has received promin® (sodium p,-p'-diaminodiphenylsulfone-N,N' didextrose sulfonate) intravenously and locally, vitamin D by mouth, calcium by mouth and oxophenarsine hydrochloride intravenously The eruption has improved about 50 per cent in the past nine months Most of the improvement occurred while the patient was receiving intravenous injections of promin®

DISCUSSION

DR ROBERT C LOFGREN I agree with the diagnosis and might mention that at the Fort Miley Veterans Hospital I have seen 4 cases of sarcoidosis recently. One of these cases showed an unusual grouped follicular eruption Microscopic examination of one of these lesions showed the typical tuberculoid infiltration about the hair follicles and the sweat glands This type of eruption is not usually mentioned in the literature as one of the manifestations of sarcoidosis

DR ARNE E INGELS I must say that the case is extremely unusual clinically The lesions had lasted long enough to produce atrophy I have not seen destructive atrophy Second, I did not see the sections which were presented Third, I failed to see the report of roentgen examinations I think the case deserves further consideration

DR ERVIN EPSTEIN, Oakland Histologic sections were presented and represented classic examples of sarcoid in the skin and in the lymph nodes As far as the roentgen examinations are concerned, the bones and the gastrointestinal tract showed nothing unusual The patient had some enlarged mediastinal glands but no involvement of the parenchyma of the lungs He is about 50 per cent better than when first seen The patient seemed to respond better to promin® than to anything else that has been tried

Granuloma Inguinale Successfully Treated with Streptomycin Presented by DR PAUL FASAL

A Case of Osler's Disease with Hereditary Telangiectasis with Tumerous Hemangiomas Presented by DR ARNE E INGELS

Frederick G Novy Jr, M D, *President*

Frances M Keddie, M D, *Secretary-Treasurer*

Oct 17, 1947

A Case for Diagnosis (Folliculitis Ulerythematosa Reticulata?) Presented by DR A A SMALL for DR W M MEININGER

Generalized Xanthomatosis Presented by DR FRANK K HAIGHT, Oakland, Calif

Multiple Idiopathic Hemorrhagic Sarcoma of Kaposi? Stasis Dermatitis? Presented by DR ROBERT C LOFGREN

Dermatomyositis Presented by DR ERVIN EPSTEIN, Oakland, Calif

Pityriasis Rubra Pilaris of Nine Months' Duration in a Woman 62 Years of Age Presented by DR FRANCES M KEDDIE

Dermatomyositis Presented by DR J M READ (by invitation, for DR WILLARD M MEININGER)

O McC, a 26 year old white American housewife, has had frequent sore throats and earaches since the age of 15 years She had taken sulfonamide drugs and penicillin frequently in the past three years One and a half years ago she first noted muscle stiffness in her arms, legs and neck, which was not associated with any infection of the upper part of the respiratory tract About four months ago the stiffness became worse and gradually increased to cause almost complete invalidism Cutaneous swellings appeared, and the skin became tight and hard and sensitive to heat and to touch The facial edema and difficulty in swallowing began three weeks ago

Numerous erythematous plaques and patches are seen on her trunk and the proximal portions of her extremities A brawny induration of the muscles seems to attach them to the overlying skin

The results of a urinalysis and a hemogram were normal The result of the heterophil agglutination test was normal The serologic reaction for syphilis was negative The roentgenograms of the chest, elbows and hands revealed no abnormalities The chemical content of the blood per hundred cubic centimeters was cholesterol 250 mg, calcium 10 mg, inorganic phosphorus 4 2 mg, total proteins 6 0 mg, albumin 4 4 mg and globulin 1 6 mg The basal metabolic rate was +13 6 per cent

A section of the epidermis and a bit of adjacent muscle showed occasional small collections of lymphocytes about small arterioles, but no eosinophils and no evidence of tissue destruction or involvement of the arteriolar walls The diagnosis was focal, chronic myositis and chronic, mild dermatitis

DISCUSSION

DR FRANCES M KEDDIE I would like to suggest the diagnosis of periarteritis nodosa The patient has had episodes of diarrhea, but none of the stools was bloody These were often accompanied with fever for about four days She has been receiving sulfonamide drugs intermittently during that period There are nodules on the ulnar aspect of the right forearm which might be compatible with a diagnosis of periarteritis nodosa This seems to belong in that group of cases in which Rich and his associates were doing experimental work on rabbits Rich administered horse serum to the rabbits and also gave sulfonamide drugs and was able to produce the lesions of periarteritis nodosa A biopsy of one of these nodules on the patient's arm might confirm this diagnosis

DR HARRY E ALDERSON It would be unusual for a person with periarteritis nodosa to survive after three years

DR FRANCES M KEDDIE More cases of chronic disease are being recognized now

DR ERVIN EPSTEIN Dermatomyositis, periarteritis nodosum, scleroderma and disseminated lupus erythematosus may be classified in a single group There is considerable overlapping between these entities It is often difficult to separate these conditions clinically

DR WILLARD M MEININGER The onset and course of this condition were characteristic of dermatomyositis The patient first noticed stiffness in her legs,

In August 1947 she had severe vaginal bleeding which required six transfusions of blood Anemia, pronounced leukocytosis and early myeloid forms were noted in the peripheral blood

On entry to the Women's Medical Ward, Stanford University Hospitals, Aug 27, 1947, she felt well, mucous membranes were clear and pale, and the skin showed isolated red papules, 5 to 6 mm in diameter, with central pustules These red papules had an indurated base and were located on the right side of her neck, under the chin, in the right axilla and on the anterior aspects of both thighs, where some evidence of old ecchymoses was visible She had palpable inguinal nodes, a 1 cm firm node in the middle of the posterior cervical chain on the left and palpable supraclavicular and axillary nodes The edge of the liver was palpable 1 fingerbreadth below the right costal margin, the spleen was not felt She had vaginal bleeding At that time the red blood cells numbered 2,900,000, hemoglobin was 48 per cent, there were 54,000 white blood cells, with 30 per cent myeloblasts and 20 per cent myelocytes, and there were 81,000 platelets A sternal puncture showed many myeloblasts and myelocytes, with a few erythroid elements

On September 4, the uterus was packed with radium (2,400 milligram hours), and the vaginal bleeding stopped

By September 10, a severe gingivitis had developed, and the patient had a daily temperature spike to 40 C (104 F) By September 15, a large, tender, purplish indurated mass, 10 cm in diameter, had developed on the right buttock, at the site of the penicillin injections, and soon similar areas developed on the left buttock and on both arms where the patient had received injections of penicillin and morphine By September 22, the indurated, well marginated swellings on the right buttock and the right arm were covered with a brownish black crust, the patient had severe gingivitis, with a number of whitish, raised, circumscribed, necrotic lesions on the oral mucous membranes, and the liver and spleen were enlarged, as were the cervical, axillary and inguinal nodes

On October 7, the red blood cells numbered 900,000, the hemoglobin was 21 per cent and the white blood cells numbered 37,200, with 38 per cent myeloblasts By this time the black crust on the right buttock had come away, leaving a brown, indurated, well epithelized plaque underneath it The purplish areas on both arms had gradually become red at the center, and the advancing margins were still indurated and elevated about 7 mm above the surrounding skin These plaques were hot and pitted on pressure A biopsy specimen was taken from this lesion on October 10, with much oozing of edema fluid and blood, which was controlled with oxycel® gauze and pressure bandages

On October 11, the blood showed a definite shift toward older forms in the myeloid series The platelet count was 72,000 On the right forearm in the region of the elbow there developed a new raised, purplish, hot area which has been gradually spreading down the forearm the past week, until it is now about 10 by 12 cm There is some scaling of the older part of the lesion, and there the purple coloring is giving way to a pinkish hue The advancing margin is a slate gray, with numerous purple petechiae The mouth has gradually cleared of lesions The lesions on the arms, while still well marginated and tense, have become brown and nontender Her temperature has come down, and the patient is brighter

On October 15, the white blood cell count was 90,000, with an increasing percentage of mature forms, the packed cell volume was 16 mm , the bleeding time was 7½ minutes, and the clotting time (capillary tube), 2¼ minutes

Treatment has included administration of pentobarbital sodium, codeine, seconal,® acetylsalicylic acid, morphine and penicillin troches; injection of penicillin in oil

I was disappointed in the results of treatment with riboflavin and vitamin A when I first used them In the absence of hydrochloric acid in the stomach, they have to be given in much heavier doses The response is always slow

DR OTTO E L SCHMIDT Riboflavin probably is specific for rosacea keratitis Patients respond to injections of riboflavin much better than to the oral administration of it

Frederick G Novy Jr, M D, *President*

Frances M Keddie, M D, *Secretary-Treasurer*

Sept 19, 1947

Recalcitrant Pustular Eruption of the Extremities Presented by DR REES B REES and DR EDWIN M HAMLIN (by invitation)

Cutaneous Hodgkin's Disease Presented by DR FRANCES M KEDDIE

O C, a white woman aged 48, was presented at the meeting of this society on Jan 18, 1947 From a biopsy of a lymph node from the left axilla the diagnosis was malignant lymphoma

A Case for Diagnosis (Psoriasis? Lymphoma?) Presented by DR FRANCES A TORREY

Lupus Erythematosus with Dissecting Pyoderma of the Scalp Presented by DR NORMAN EPSTEIN

Acrodermatitis Perstans Presented by DR ROBERT A STEWART

Vegetative Pyoderma Controlled with Streptomycin Presented by LIEUT COL ROBERT S HIGDON (by invitation)

Pemphigus Vulgaris Presented by DR REES B REES

Superficial Epitheliomatosis Presented by DR GRANT MORROW

DISCUSSION

DR H V ALLINGTON, Oakland In one case I prescribed podophyllin in isopropyl alcohol The patient was asked to use it daily if the reaction was not too severe It could not be applied every day because of irritation and soreness When the reaction became annoying, the patient would interrupt the treatment for a few days and then resume it When I last saw him the lesion had undergone involution to a great extent

Urticaria Pigmentosa in an Adult Presented by DR LEO COLUMBUS, Berkeley

Urticaria Pigmentosum Presented by DR ERVIN EPSTEIN, Oakland

Acrosclerosis Presented by DR GRANT MORROW

J M, a white man aged 42, was admitted to the Southern Pacific Hospital in August 1947 He complained of dull intermittent pain of two years' duration in

Archives of Dermatology and Syphilology

VOLUME 60 DECEMBER 1949 NUMBER 6

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ROLE OF EMOTION IN DISORDERS OF THE SKIN

O SPURGEON ENGLISH, M D
PHILADELPHIA

WHAT emotion plays a role in disorders of the skin is a fact accepted by most, if not all, dermatologists This fact has been well elaborated in the literature, both by those specializing in the field of dermatology and those in the field of psychiatry who have joined with dermatologists in thinking through some of the complicated disease conditions within that field of endeavor

The psychosomatic approach to any disease makes a much greater demand for knowledge of causes, pathologic processes and procedures of treatment than any single newly discovered disease This is because a whole new system of dynamic forces, emanating from the mind, which act as toxic agents, must be known and understood Emotions can be helpful phenomena in the life of man, but they can also be harmful and make him sick These emotions must be understood as causes of symptoms, with some ability on the part of the physician to assess and weigh them quantitatively It must be known what kind of pathologic changes they will produce and also how therapeutic manipulation of these emotions will cause them to lose their capacity for producing end results of disease in the skin Before passing to the role of emotions generally and what they can do, let us see what the commoner emotions are which are prone to be causes The most commonly encountered emotions are the following

1 Need for love (approval, appreciation, recognition)
2 Anxiety (fear and worry)
3 Hostility (anger, hate, aggression)
4 Inferiority feelings
5 Ambivalence
6 Guilt
7 Ambition (competition)
8 Envy

NEED FOR LOVE

The need of love is one of humanity's greatest hungers, and many other emotions are dependent on it From the cradle to the grave human beings struggle under it Some of them have a great hunger for love

From the Department of Psychiatry, Temple University School of Medicine

DR PAUL FASAL I agree with Dr Ostwald that this is a case of acrodermatitis chronica atrophicans The patient was born in Austria, a country where such cases seem to be much commoner than in this country A case of poikiloderma vasculare atrophicans of such long standing would resemble a roentgen dermatitis and not only show atrophy

A Case for Diagnosis (Periadenitis Mucosa Necrotica Recurrens?) Presented by DR ERVIN EPSTEIN, Oakland

A Case for Diagnosis (Pigmentation and Atrophy of the Face and Neck, Lupus Erythematosus?) Presented by DR H V ALLINGTON, Oakland

Localized Scleroderma Presented by DR ARNE E INGELS

A Case for Diagnosis (Angioma Serpiginosum?) Presented by DR H V ALLINGTON, Oakland

Sarcoidosis Presented by DR ERVIN EPSTEIN, Oakland

J C A, a 27 year old Negro, was first seen on Dec 16, 1946, because of an eruption on his face, neck, elbows, knees, perianal area and penis The condition started with parotitis in January 1943 This was followed by joint pains for which he was hospitalized in an Army hospital Investigation revealed roentgenologic evidence of enlargement of the mediastinal lymph nodes and parenchymal infiltration in the lungs The tuberculin reaction at this time was reported as "questionable" His electrocardiogram revealed inversion of the T wave in the first lead While he was in the hospital, generalized lymphadenopathy, cutaneous nodules and iridocyclitis developed Biopsy of a lymph node was said to have showed the histologic picture of sarcoid

When first seen, nearly four years after the first attack, he presented multiple discrete and coalescing nodules in the aforementioned locations The lesions were elevated, firm, nontender and in some instances umbilicated On the face particularly, the nodules were grouped around the eyes, nose and mouth Lesions were present on the nasal mucous membrane There was enlargement of the cervical, posterior cervical, supraclavicular, inguinal and axillary lymph nodes Corneal opacities were present

The biopsies from the skin and the lymph nodes showed epithelioid tubercles without caseation and occasional giant cells in the derma which were considered diagnostic of sarcoidosis

Numerous blood cell counts gave essentially normal findings Results of multiple urinalyses were normal Intradermal tuberculin tests elicited negative reactions to both the first and the second strengths Six Kahn tests gave positive reactions One Kolmer test gave a positive reaction, two were doubtful and one negative His wife is being treated for latent syphilis The total blood proteins were 6 9 mg per hundred cubic centimeters, the albumin being 2 72 mg and the globulin 4 18 mg Results of six blood calcium tests ranged from 12 to 14 mg per hundred cubic centimeters Nasal scrapings did not reveal acid-fast bacilli Roentgen studies revealed a few indefinite nodules in the upper lung fields and enlarged noncalcified nodes in both hili Roentgenograms of the hands, abdomen and lumbar vertebrae were normal Electrocardiograms showed diphasic and negative T waves in the four chest leads, indicating myocardial damage

concentrating on the feared thing, in the hope that by this wariness it can be averted, too little energy is left for happy living If this phenomenon goes on long enough and severely enough, the body can no longer function properly and symptoms of illness have arrived These come through the mechanism I have already described, by which emotional energy is converted into somatic disturbances through the autonomic nervous system We then have psychosomatic symptoms

HOSTILITY

Like the need of love, hostility is also ubiquitous Without spending too much time on the philosophic theories of the origin of hostility, let us say simply that when the human organism fails to find conditions which keep him in a constant state of well-being, he experiences an unpleasant emotion accompanied by ideas of retaliation and the use of force to gain his ends, even of destruction of the person or thing which makes him uncomfortable or which thwarts him This we call hostility It is impossible to conceive of any one in our society without any hostility whatever, but certainly small amounts can be present without too many untoward results This is true, especially if the modicum is properly blended with the rest of the personality to produce wit or zestful, spicy conversation or if it results in a wholesome competition "Get up and git," or "I'll show them," is an aggressive philosophy, which contributes to progress individually and generally But, unfortunately for society, a great deal of hostility does not take this form It does not even find vent in occasional outbursts of anger, righteous or otherwise It has to be held in check, because the child or the adolescent does not feel that his environment will tolerate any show of hostility He fears rejection or punishment, so his holding in results in repression a "burying alive" process of which the mind is capable The buried or repressed hostile activity builds up, and the more it builds up, the more labor another part of the mind has to exert to keep it from breaking out While this battle is going on there is much less energy available for friendly relations in other directions In fact, the person having this internal struggle becomes guilty about his state and not only feels no impulse toward loving but thinks that he does not deserve to be loved The results of this continual psychopathologic engrossment may be various things, one example being the obsessive thought that he will harm somebody However, we are more interested in where the hostile activity that builds up within expresses itself somatically We discover that it goes in several directions to produce disturbances of the upper and lower gastrointestinal tract and enuresis, headache, ticlike movement, probably epilepsy and disorders of the skin, and plays a role in vascular hypertension and other disorders Actually the effects of these

A Case for Diagnosis (Parapsoriasis? Dermatitis Medicamentosa? Vitamin A Deficiency?) Presented by DR A A SMALL for DR O E L SCHMIDT, San Mateo, Calif

A Case for Diagnosis (Lupus Erythematosus? Senear-Usher Syndrome?) Presented by DR A A SMALL for DR W M MEININGER

A Case for Diagnosis (Xanthoma Sine Diabetes? Necrobiosis Lipoidica?) Presented by DR ARNE E INGELS

Two Cases of Epithelioma Adenoides Cysticum, in Mother and Daughter Presented by DR ARNE E INGELS

N M, the mother, is 79 years old She has tumors ranging in size from 0 5 cm up to 3 cm on her chin, face and back The tumors are light pink or red, firm to touch, embedded and not painful Many of them have a semitranslucent appearance None is ulcerated There are no café au lait spots The patient gives the impression of average intelligence The tumorous masses have been developing gradually since as far back as she can remember The patient has always been in excellent health

A biopsy, performed Oct 15, 1947, showed epithelioma adenoides cysticum

A B, the daughter, who is 15 years old, shows ill defined nodules densely studded on the midline of her face, nose and forehead and on her extremities Some of the nodules have a reddish pink appearance with a capillary design The great mass of them are colorless, firm and waxy in appearance The front of the right thigh shows a partly pedunculated tumor, vivid red and sensitive, but not inflamed

She has always been healthy, and her intelligence is about average

A biopsy, performed Oct 15, 1947, showed typical epithelioma adenoides cysticum

DISCUSSION

DR H V ALLINGTON, Oakland, Calif I thought both cases very remarkable I did not realize that nodules of the size that the older woman presented occurred in this disease

DR ERVIN EPSTEIN, Oakland, Calif The lesions are similar to those seen in tuberous sclerosis and adenoma sebaceum It is often brought out in discussions that these diseases are related

DR ARNE E INGELS The lesions are not unlike those of tuberous sclerosis, without the typical sclerosis The accepted name for the cutaneous lesions is epithelioma adenoides cysticum Sections which I expected to be ready were not I have seen cases in which microscopically the nerve elements were interspersed with the usual elements and collagen The very unusual tumor formation which you see in this case I have seen many times previously

A Case for Diagnosis (Leukemid? Purpura Urticans?) Presented by DR. A A SMALL for DR O E L SCHMIDT, San Mateo, Calif

E J, a 46 year old housewife, was well until June 1947, when she began to have weakness, soreness of her mouth and some purpuric spots on her extremities

living up to expectations This emotion can kill the joy of living and may cause the patient to adopt a life of excessive self-sacrifice, which in the course of time produces physiologic disturbances As an emotion it acts to block the reception of impulses emanating from others of love and approval Starvation of the love needs can occur from guilt and the pathophysiologic results in the way described earlier

AMBITION (ENVY, COMPETITION)

The ambitious person does not necessarily have pathologic emotions, but he certainly runs the risk of being infected with envy or excessive competitiveness These emotions tend to produce tension, and the professional, financial and social success of many people has been paid for at a high price, i e., the price of tension, which is prone to express itself through the nervous system on many parts of the body The aggressive component inherent in these emotions plays a large role in such conditions as cardiovascular disease, migraine and vascular hypertension, and to some degree in many others A successful person can have achieved his goal by great ability and a friendly, easy-going manner, but he is in the minority Ambition with its attitude of competition, sometimes accompanied by envy, is all too often carried along as unnecessary equipment on the road to successful service

With this section I conclude these brief pictures of the more common and important emotions which are going to affect the skin, if emotion is playing any role whatever

HOW THE EMOTIONS AFFECT THE SKIN

Since emotions will find expression in any or all parts of the body, it is inevitable that so important an organ as the skin should be affected Probably the greatest number of ideas relating to man's actions and feelings are spoken of in reference to the heart The stomach and bowel run the heart a close second, but the skin will not be too far down the list When, for instance, a man does anything free of blameworthy motives, we allude to him as acting "with a whole skin" When we escape injury, we "save our skin" Cheating or taking advantage of the other fellow is to "skin" him To be oversensitive is to be "thin-skinned" and to be relatively impervious to the attitudes of others is to be "thick-skinned" The expression "you are a scab" or "you give me the itch" are well known and indicate the response of the skin to hostility "I blush for you" means "I identify myself with you and disapprove of you" Such expressions indicate that the skin is a potent carrier of emotions and attitudes Just as the stomach may act in a perverted way when the personality is unable to cope with a problem, so the skin may do the same Our first impression was that emotion was slower to appear in the skin than in the heart or the gastrointestinal tract, but

and wax U S P, 300,000 units daily, from August 27 to 31, and of aqueous penicillin from September 9 to 20, administration of pyridoxine, and numerous blood transfusions At present cold packs are being placed on the tender plaque on her right forearm

Examination of the sections showed large primitive cells resembling large macrophages

DISCUSSION

DR REES B REES I should suggest ecchymosis of the type often seen in leukemia, although histologically there was no definite leukemic infiltration

DR HARRY J TEMPLETON, Oakland, Calif The diagnosis, I think, is very clear There is leukemia with hemorrhage into the skin I should like to discuss this case from the standpoint of a possibly valuable new therapy, helpful to my associates and me in a single case A couple of years ago there was referred to us in Oakland a patient with chronic myelogenous leukemia, the diagnosis was proved by an internist and a hematologist Blood counts going back a number of years showed that the case was a rather typical one Generalized erythematous dermatitis, which became extremely severe, developed The patient had had about every type of orthodox therapy, without benefit I had read an abstract at about that time in which colchicine had been pointed out as having something to do with the cell mitosis It is used by planters for treatment of seeds of plants and seedlings of plants, whereupon certain changes result in the production of entirely new varieties of the plants

We gave this patient colchicine, 1/100 grain (0 5 mg) tablets, every three to four hours to the point of tolerance, that is, until the patient got nausea, abdominal cramps and diarrhea At that time the dosage was dropped to one or more tablets a day, the number depending on how well the drug was tolerated The cutaneous lesions began to improve and then disappeared after the patient had taken colchicine for two months About two weeks ago, at my request, Dr Paul Michael rechecked the blood count He stated that the man still had the hematologic picture of myelogenous leukemia, but that something had happened, there was a decided improvement in the blood picture, with less immature cells and more approach to maturity in the cells

Drs Lunsford, Allington and I have been seeking more cases of that sort Through the kindness of Dr Torrey several patients showing lesions of the lymphoblastoma group have been started on colchicine treatment at the University of California Clinic

DR FRANCES A TORREY At the present time I do not feel that my associates and I have anything definite to report We have 3 cases diagnosed as mycosis fungoides One of them we have been following for a long time Biopsy of the skin in each confirmed the diagnosis The patients in 2 cases have been able to tolerate colchicine in a dosage of 1/100 grains three times a day But so far there has been no definite improvement However, because of the characteristics of the disease, I think it is too soon to give a report

DR HARRY J TEMPLETON, Oakland, Calif At my request Dr Leslie Smith of El Paso, Texas, started treating a patient with a lymphoblastoma with colchicine This patient responded dramatically at first, and then the condition apparently flared up The dose was increased, and I am waiting to hear Dr Smith's report of the outcome

DR JAMES R DRAKE I should like to ask Dr Templeton whether he is interested in using colchicine in treatment of other diseases of the lymphoblastoma group

DR HARRY J TEMPLETON, Oakland, Calif Yes

lowing 'What is your skin trying to say for you?" or "What is there of your inner self which is revealing itself through your skin?" or "What is your skin expressing?" or "What do you suppose your skin is acting out?" The physician has to be very comfortable with the idea that personal feelings and experiences will use body organs for expression Only when the physician believes that such things can happen and is personally comfortable in his own thinking about these concepts, can be bring the patient to make his contribution in treatment cooperation

NEUROPHYSIOLOGIC CONNECTIONS BETWEEN EMOTION AND SKIN DISEASE

Now it is unlikely that there is any symbolic expression of ideas or attitudes anywhere in the body which does not utilize nerve pathways, vascular changes, chemical alterations and structural tissue changes as the medium for transmitting the message In some cases the psychic stimulus acts over a short period and then wanes in strength or is neutralized by a counterphenomenon, as, for instance, the homesick man or woman who is able to return home In other cases the stimulus acts continuously over a prolonged period and is neutralized with difficulty or not at all

Having enumerated the emotions and in a general way indicated their mode of action, let us turn to the emotional states in which we encounter a linking of emotions and skin problems

NEUROTIC EXCORIATIONS

As knowledge of human emotional needs and how they are met increases the line of division between what is neurotic and what is psychotic becomes less important There is a pattern of wholesome development of personality and adaptation, and if this pattern is not approximated the many devious by-paths of attempted solution are almost legion In neurotic excoriations, for instance, the patient may already be suffering from delusions of parasitosis before the behavior which produces the excoriations begins Even if delusions are not present there is a strong need to disfigure, to suffer pain, to call attention to the self, to seek attention in a perverse way because the more healthy wholesome way was never discovered and firmly established early in life The wholesome pattern of training tends toward beauty, culture and the esthetic satisfaction of others This brings rewards of ego satisfaction, but if they are unknown to the patient and if he knows and seeks pity, shocked surprise, anxious concern or even revulsion and condemnation, he nevertheless accepts this reaction in others rather than being a complete nonentity in their eyes Most people cannot stand being ignored, and self-mutilation producing an unsightly skin,

but either have no recognition of what they need or have no technics for obtaining it Lack of it brings such untoward emotions as frustration, hurt pride, envy and jealousy Others have perverted and symbolic ways of obtaining it through excessive use of alcohol, food, sex or drugs Others know they need affection, attention and rewards, and they take the conventional kind of actions and responsibilities which bring them the love they need and its derivatives of approval, appreciation and recognition Thus, to be assured of love is a most important emotional need and sufficient gratification of this need is of the greatest importance to health, both physical and mental

There has been a general reluctance to accept the proposition that love is an actual necessity for health and happiness As a health factor it has not had the same scientific standing as the chemical symbol for iron, for example, but the more one studies man and his various illnesses, the clearer it becomes that he can live neither a healthy nor a wholesome life without it

ANXIETY

Anxiety is one of the earliest emotions aroused and one of the most basic in the whole life of man Fear is its conscious representative but the origins of anxiety itself are largely unconscious We have to use the word "fear" in order to describe the origins, since anxiety arises predominantly out of two early life situations, namely, fear of physical harm, pain or injury and fear of the loss of love When the child is threatened with the loss of his mother's protective presence, he sustains uncomfortable sensations, in both the mind and the body, and in describing his reaction to this situation we say he fears a loss of love (meaning the loss of a friendly presence) Also, as the child comes to suffer pain from falls, bumps, rejection or punishment, he dreads its repetition Its possibilities of repetition fill him with the same uncomfortable sensation, and we call this sensation anxiety Anxiety has two components one of them being psychic and distressing to the mind in a varying degree The other, the somatic component, arises from the fact that once the distress of the psyche has reached the threshold of action the emotional energy overflows by way of the autonomic nervous system to any or all parts of the body People who in the ordinary course of life suffer from too much anxiety are people who in early life lacked a consistent supply of a reassuring, friendly presence or who were subjected to too many real pain-inflicting experiences or threats of them This allows a dread or a worry pattern to construct itself, and as life becomes more complex the things which threaten deprivation of love and security or real physical distress increase in number

Not only does the emotion of anxiety impair one's ability to enjoy life, but it has more far-reaching effects If one's energy is used up in

the symptoms may have nothing to do with immunologic allergy They feel that psychologic elements do not produce immunologic allergy but that in many patients similar symptoms may certainly not be the result of immunologic allergy Such patients who are not allergic in the immunologic sense would, we assume, have this sensitivity of skin in the same way that some patients have a most labile heart action, others have a sensitive stomach and others are sensitive sleepers We are especially indebted to Miller and Baruch for including in their study a control group of children Further studies of this kind with controls are much needed in this field of our mutual interest This would mean that when the child or the adult was under stress or when the relationship of the child and the mother or her substitute was endangered, the skin would be vulnerable to symptomatic reactions [2] Certainly, we observe frequently enough inflammation, itching and weeping of the skin in eczema when the patient is going through some environmental stress, which places him in a position of responsibility where he feels alone and unprotected Then he has a longing expressed in the skin by itching which calls for the soothing hand (The hand which scratches is the soothing hand, temporarily at least) He cannot weep, but his skin weeps for him Eczema patients are usually depressed and long for love, but they can't use love when they get it It may even tend to aggravate them They long to scratch instead, but they are only the more aggravated by scratching After all, love has been defined as "an itch one can't scratch" So far as itching may represent a desire for love, certainly scratching is an unsuccessful attempt to obtain it

PRURITUS ANI AND VULVAE

A later period of emotional fixation would be when in the course of psychosexual development, the potential pleasure for sexual excitement and orgasm never fully reached the genital region It remained in the anal region and scratching served the role of a sexual excitement, instead of the mature genital pleasure Pruritus ani and vulvae is not always psychologic in origin, but a psychologic factor doubtless plays a contributing role in many cases That this is true does not preclude some capacity for normal sexual function in the individual with the condition The case is not, in other words, one of a normal or a perverse way of sexual gratification, but it can include a little of both, and this should be investigated as a possibility in each case of pruritus More than one patient has said such things as the following about pruritus, "It's like being excited sexually, only one is never able to achieve an orgasm It's only excitement and tension and no let down"

2 Saul, L J Relations to Mother as Seen in Cases of Allergy, Nerv Child 5·332, 1946

forces of which people individually appear so unconscious have long since been noted by them in general in that they observed that situations gave them "headaches" or "made them sick," or they "itched for a fight" and "got their blood pressure up" over something frustrating Since people are not proud about being irritable, disagreeable, unpleasantly aggressive, arrogant, demanding, tyrannical or domineering, they remain remarkably unconscious of the hostile motivation But there are tremendous quantities of hostility latent in the human race, producing not only serious social problems but many individual symptoms of illness as well

INFERIORITY FEELINGS

To many it might appear that feelings of inferiority could exist as a social phenomenon but not one with any medical implications But feelings of inferiority are closely linked up with the basic emotions of love and hate Obviously, the person having feelings of inferiority has not had enough acceptance and appreciation There are few people who ever feel quite satisfied with themselves, but in some persons the feeling of worthlessness can be so deep as to destroy the capacity of the psychic apparatus for maintaining physiologic equilibrium Once a feeling of inferiority is deeply set, it is not easy to restore the self-esteem to a proper balance

AMBIVALENCE

"Ambivalence" is a term given to the condition of directing both love and hate toward a person or the world in general These impulses may be present practically continuously and show themselves rather subtly, or they may show themselves more superficially and plainly by a capricious change of mood and attitude, in which those associated with them are loved one hour or one day and hated and condemned the next We see a man, for instance, who protests how much he loves his wife but never listens to her requests, her suggestions, never tries to further her plans and never helps her in any tangible way We see a woman who protests that she loves her child but who never allows the child to do anything he enjoys and never lets him decide anything for himself This mixture of emotions which has the descriptive term of ambivalence, which portrays it as one emotion, can, like guilt, block off the benefits of straightforward, friendly, satisfying and wholesome human relations

GUILT

Guilt is an emotional distress resulting from criticisms voiced by the conscience, the conscience being a well preserved memory pattern of what the parents or substitute mentors said was right and proper The person undergoing guilt has reason to feel that he has not been or is not

TRICHOTILLOMANIA

Trichotillomania is likewise not really a condition of the skin but a piece of neurotic behavior What one sees in the hairy regions are the end results of a compulsion to extract the hairs forcibly with the fingers or other means This unusual behavior starts as a perverse means of gratification, of producing, in other words, pleasurable pain Those whose behavior is of this sort are in the class of those who bite and pick the nails until the nails are painful and bleeding, crack their finger joints, stimulate the gums with toothpicks or other instruments until the gums bleed or who squeeze and press comedos until they have produced macerated areas and bruises Tugging at ear lobes, biting the lips or pinching the skin are other manifestations of efforts to produce a pleasure-pain effect on the body, because more natural and wholesome ways of relieving tension either have not been permitted or have not been taught early in life They play with themselves, stimulate themselves and usually disfigure themselves, mainly because the activity gratifies This fact is hard for average people to understand, but it is no more enigmatic than the fact that people consistently eat or drink more than is good for them In either case they (1) indulge themselves in something they enjoy, (2) they relieve tension at the moment, (3) they put themselves at a disadvantage in the eyes of others through it but (4) there is an insistent urge to repeat it for the momentary pleasure it produces From this description its sexual component can be seen To cure it, the physician has (1) to help the patient to endure the tension on cessation of the habit and (2) to get the energies channeled into more wholesome and useful directions

HYPERHIDROSIS

Excessive sweating of the hands, axillas and feet is fairly common. It probably could not be settled at the present time whether there is any inherent pathologic condition of the sweating mechanism or whether this manifestation is entirely emotionally conditioned There is considerable evidence for the latter There seems every reason to believe that the sweat gland mechanism might have as wide variation in function as the glands in the mucous membrane systems of the stomach, the intestine and the respiratory and genitourinary tracts One must grant that there is wide variation in the outpouring of secretion in these areas, and the skin response could be just as labile We see analogies in sphincter control, where in states of fear people cannot "hold their water," and it drips from the hands, axillas and feet and often other parts of the body as well Whether there is any wisdom of the body in this mechanism, that is, whether there are any conditions under which

in blushing and sweating we have very prompt phenomena which sometimes are distressing to a repressive patient Also, urticaria and allergic phenomena have a high incidence and can make their appearance quickly Hence, so far as these two phenomena often have a large emotional component, we cannot say that the skin differs from other organs because it does not respond promptly Dermatology and psychiatry share the phenomenon of having a few acute conditions and many which are slow to improve Now the skin undoubtedly is like other organs in that it may symbolically represent an inner attitude In other words, the skin may give one away The well known phenomenon of blushing embarrassment indicates "I believe you know what I'm thinking and I'm afraid and ashamed" The blush symbolizes inner excitement with fear of exposure being prominent, the exhibitionistic wish, however, triumphs over fear and shame, which would try to keep these emotions hidden

But the skin, in addition to "burning" with shame, may weep out of sadness So just as there may be an idea quickly speaking its message by way of the skin, so long-continued tensions make themselves known through activity of the autonomic nervous system In adolescence, for instance, there are many conflicting feelings of being good and bad, of being attractive and ugly, of being clean and dirty, of being intelligent and stupid, all at the same time The restless longing for attention makes them latently strongly exhibitionistic It is a paradox that at the time they wish to be most presentable, attractive, lovable, beautiful, they are affected with acne or some other disturbance of the skin But if we grant that emotions affect the function of the skin at all, then it becomes plausible that they must show their worst side through disease of the skin Both children and adults may expose their worst behavior in a bid for attention The skin may take over this action What we must keep trying to do if we are to be successful in understanding the language of psychosomatic disease is to remember that the skin can act a certain way or act out a problem, just as the whole person may act through voluntary muscle activity

Since most physicians pride themselves on being practical men, these ideas may sound impractical and fantastic to many However, the practice of psychosomatic medicine requires that the physician use other aspects of his education than physics and chemistry It requires that he (1) utilize what he knows or can learn from the poet, the story writer, the artist and the philosopher and (2) bring this knowledge to bear on his patient's approach to the symptoms in question This approach seems less reliable and is certainly less tangible than remedies which can be taken internally, intravenously, intradermally, intramuscularly or by unguentation It takes a great deal of understanding and self-confidence to ask the patient some such question as the fol-

from a study of 100 cases that the patients were of the driving, high tension, competitive type, keyed to high pitch and perpetually intent on a destination to be achieved at no matter what expense Saul [6] seemed to find that longings for love frustrated through fears of sex in persons with a highly erotized skin were responsible for attacks Both observations have the common denominator of intense longings for achievement of gratification If we keep in mind that there are many hard-driving people who long for things without getting urticaria, but that it is this type of personality which furnishes the final factor that sets the symptom complex into motion, and that this factor can be treated and tension in this direction lowered, we have done the most fruitful thing possible toward relief of the symptoms

SEBORRHEIC DERMATITIS

Ingram [7] in 1939 called attention to the emotional instability of those suffering from seborrheic dermatitis by stating that it could vary from the sullen, sulky indolence of patients who present some of the heavier forms of acne to the high-strung overactivity of the patient with rosacea "States of anxiety, stress, and strain are conditions which the seborrhoeic will not readily tolerate" Ingram studied 100 seborrheic patients and found them hard to study, as they were not easy talkers and were afraid of persons in authority They were shy and solitary and had trouble in social contacts When with people they felt lost, exposed, uneasy and tongue-tied They could not stand hostility toward themselves They were compulsive workers and perfectionistic They were sensitive and felt inadequate As might be expected from such traits, they were unaggressive and overcompliant No follow-up treatment is reported, but it could be assumed that any cutaneous symptom present with such marked disturbances of personality should improve under effective therapy

The same author studied patients with psoriasis and found no specific type of personality, but concluded that the proportion who were maladjusted was far in excess of the proportion of such persons in the general population

As the role of emotions in cutaneous conditions becomes more widely accepted, we shall have more psychotherapeutic efforts and hence more reports of results of treatment This will be good for the morale of both dermatologists and patients alike As things stand, the patient still has too little faith in what can be done for his condition by a psychotherapeutic approach It is really hard for him to look at his emotions,

6 Saul, S J, and Bernstein, C The Emotional Settings of Some Attacks of Urticaria, Psychosom Med **3** 349, 1941

7 Ingram, J T The Seborrhoeic Diathesis, Brit M J **2** 5, 1939

like a social act of bravado, is preferable in certain egos to the emptiness of oblivion If delusions are present as the basis of self-inflicted excoriations which follow, we should, instead of speaking of the role of emotion in skin disorders, speak of the invasion of morbid ideas when healthy emotions and ideas are absent Happy people, i e, people with a sense of well-being, tend to seek out others and join in mutually pleasurable behavior It is when this sense of well-being is absent that an individual falls back on himself, feels himself, "tunes in on himself" to use the expression of one patient and falls prey to ideas of something morbid or unhealthy in his skin or some other part of the body

DERMATITIS FACTITIA

In dermatitis factitia we see the patient secretive about his goal He wants attention, but one must be a detective and guess he wants it He even tries out one's diagnostic acumen like the children in New York who recently ran away from home and hid in a cemetery and when found by detectives said "we just wanted to see if you were any good at your business" The patient with dermatitis factitia seems to enjoy challenging the physician to make a diagnosis for the pleasure of being enigmatic (to see if the physician knows the business of understanding people) before the real question of the motive of self-mutilation ever becomes an issue

EMOTIONS AND SKIN SENSITIVITY

Eczema There is increasing evidence that maternal rejection plays a large role in psychosomatic conditions, just as in neuroses and psychoses [1] In fact, we do not mean to distinguish between these three divisions of emotional conditions too sharply, for clinically they merge as different manifestations of the same basic emotional and ideational difficulties each merely having its own pattern and intensity This maternal rejection with its absence of affection to meet the minimum needs of love seems to leave the skin organ in a state of sensitive irritability or easy vulnerability to internal emotional conflict or external pressures or deprivations, just as the same conditions disturb heart action and normal function of the gastrointestinal tract or even prevent restful sleep Without the buffering or protective effect which a restful, secure relationship with the mother produces, we have a skin which might be subject to eczema or urticarial symptoms without there being an immunologic allergy in the patient [1] Miller and Baruch make a distinction between patients in whom asthma, hay fever, eczema and urticaria may have immunologic allergy as their source and those patients in whom

1 Miller, H, and Baruch, D D Psychosomatic Studies of Children with Allergic Manifestations, Psychosom Med **10** 275, 1948

OLD DERMATOLOGIC DRUGS WHICH SHOULD BE RETAINED

MARCUS RAYNER CARO, M D.
CHICAGO

WE ARE living in the "Golden Age" of dermatologic therapy, or so it would seem During the decade since sulfanilamide was first introduced into therapy a procession of new potent drugs has been added to our weapons against disease With the sulfonamide compounds in all their many variations, with penicillin, streptomycin, tyrothricin, bacitracin, aureomycin and other antibiotics yet to be named, with the vitamins in all their fractionations, with radioactive isotopes, and with the host of antihistaminic drugs it would seem that the therapeutic progress in these few years is unmatched in any period in history Only time and the merciless inroads of experience will tell whether these contributions will live through the ages as permanent achievements, as have the artistic wonders of the "Golden Age of Pericles"

It is unfortunate that all these drugs have appeared on the scene as "wonder drugs" Such an introductory appraisal is not conducive to the competitive emergence of a drug of permanent value Each drug was wishfully accepted as a miracle and at once was utilized in every conceivable disease It was only after mishaps, complications and failures that the faith in miracles was shaken and was replaced by the cold, analytic scrutiny that should be the challenge of all new drugs. There is much evidence already on record that not all the advances made by the use of these new drugs are permanent steps forward In the problem of infectious diseases there is a continuous adaptation of the micro-organisms, which in time prevents their complete annihilation Many of these drugs produce sensitizations or other toxic reactions which make their continued use hazardous It is true that all the new drugs are being constantly developed and improved While improvement is always a sign of progress, it is nevertheless also an indication that there are deficiencies that need correction

In times like these, when to the casual observer we dermatologists seem to be moving from success to success, it is well for us to look backward, to appraise the past and to hold fast to what is good In

Read at the Seventh Annual Meeting of the American Academy of Dermatology and Syphilology, Chicago, Dec 9, 1948

These conditions are not actually cutaneous conditions but psychiatric conditions and severe ones at that, but since their nature is such as to bring them to the attention of dermatologists, some discussion of them seems pertinent in a paper of this kind Just as maternal rejection may sensitize the skin to minor or major departures from peaceful and quiet functioning, so the same state of affairs prevents an emotional buffering from morbidness of mood When a person feels unloved and does not have the interest of those who have power and wish to protect with that power, ideas spring up in the mind of destructive forces invading the organism In childhood it is the bogeyman or wild animals, while in adulthood it is the undue suspicion of burglars and violence or of invasive cancer or syphilis Syphilis or cancer is merely the later life formulation of the bogeyman or the wild animals In either case, pain, destruction of tissues and eventual annihilation are felt to be the end result In phobias there is a great distrust born of real events in early life which would normally evoke distrust There are guilt and feelings of unworthiness There is great difficulty, amounting to almost complete inability in some cases, to trust and believe in the one who would help them Out of a long-carried-over feeling of guilt they think, "I should be the victim of a destructive disease I deserve no better fate Something dreadful must happen to me to even the score I am being, or I will be, punished for my wicked thoughts and acts" In therapy the task is to have the patient feel a warmth toward others and a joy in doing for others, so that he begins to reestablish a feeling of worthiness This must provide the ground work for interpretation of the symptoms No belief in a worried person is senseless Every belief has a cause in some earlier experience There is not necessarily one thought or fantasy which, if discovered, enables the whole neurosis suddenly to disappear This happens only rarely In these cases most of the results depend on slowly enriching the empty emotional life, which has left room for morbid ideas, and coming to an understanding of why a painful thought like that of having cancer or syphilis can serve any purpose It serves to atone for some childhood misdeed or "bad thought" Only when this is understood and the patient can forgive himself, can he understand how to have a life free of the burden of constant preoccupation with such distressing thoughts Some of these patients improve and get well with a few psychotherapeutic interviews—three to six in number Most of them, however, if their disease is of more than six months' duration, need longer, more intensive psychiatric treatment and should be referred to a psychiatrist for treatment if feasible These cases can be among the most difficult in the field of psychiatry

Nearly every dermatologist of experience has his pet remedy for each dermatosis, a drug tested by time and countless usages and at times inherited from his preceptor While the use of some of these remedies may represent wishful thinking and unwarranted enthusiasm, often it represents the product of careful observation of cause and effect by good clinical observers, whose experience should not be lightly brushed aside In the practical management of a dermatologic patient it is helpful for us to keep all these remedies in mind Far too often we dermatologists exhaust all methods of treatment which are indicated on rational grounds and in the end come up against the stark fact that our patient has not been helped at all It is helpful at such a time to be reminded of drugs that empirically and often without logical justification may succeed in giving the patient at least symptomatic relief

DRUGS FOR INTERNAL USE

Of the drugs used internally arsenic compounds probably have the oldest history and the most varied career from generation to generation Centuries ago they were used as a remedy for asthma For many years they fell into disuse medically because of frequent employment as a poison In the seventeenth and eighteenth centuries they were used medicinally only by quacks for treating fever and ague One of these quack preparations was so successful that a Dr Fowler had it analyzed and published the prescription in London in 1786 The use of Fowler's solution (potassium arsenite solution U S P), as it has since been known, helped to raise arsenic compounds again to a status of medicinal respectability One need not discuss at length the importance attained by arsenic compounds with the introduction of arsphenamine ("salvarsan") by Ehrlich for the treatment of syphilis This importance was enhanced by the later development of neoarsphenamine (neosalvarsan®) and the more recent oxophenarsine hydrochloride (mapharsen®) At one time or another arsenic compounds were employed in the treatment of nearly all dermatoses They undoubtedly have some beneficial effect in many diseases Their general use was soon limited, however, by the recognition of their occasional harmful effects, such as keratoses, epitheliomas, arsenical dermatitis and visceral complications In the treatment of syphilis, however, arsenic compounds long remained unchallenged With the advent of penicillin, it seems at present as if arsenical drugs will be replaced completely even in the treatment of that disease Only time will tell whether treatment with penicillin, effective as it is in quickly rendering a syphilitic patient noninfective, will need to be followed by chemotherapy in order for one to obtain the highest possible percentage of long range cures or remissions

Arsenic compounds are still being used frequently in diseases other than syphilis Neoarsphenamine and oxophenarsine hydrochloride are

this would be advantageous is unknown to us MacKenna [3] suggested that "a patient suffering from pompholyx may be indicating by a psychological mechanism that he cannot use his hands and feet" However, in psychiatry, when hyperhidrosis is an accidental symptom of an otherwise more inclusive neurotic pattern, we frequently find that in the course of gaining the security which cures the other symptoms, hyperhidrosis ceases In this connection, Wittkower,[4] in a study of 50 patients with pompholyx, found them to be unusually narcissistic, and four-fifths of them had shown other outstanding neurotic symptoms prior to or at the time of onset of the condition He found them vain and affected in their manners and speech They were ambitious but afraid of failure They were afraid of getting hurt physically and emotionally They were afraid of exposing their own feelings to others If severe hyperhidrosis exists alone as the main complaint and is unresponsive to local treatment, psychotherapy should surely be utilized As in blushing or more particularly the fear of blushing (erythrophobia), the patient may be reluctant to spend the time necessary to get at the emotional basis of a symptom which appears simple in nature but actually has a great deal of psychopathologic material underlying it Should the patient decide to undergo intensive psychotherapy for a symptom like pompholyx or erythrophobia, there is no question but that his personality would derive great benefit as a result of the changes he would have to make to get rid of his symptom The patients rarely realize that they need to get any help with their personality, generally feeling adequate in this area However, in making this need clear to the patient we may help him to decide that the treatment for the removal of just one symptom, which at first glance looks tedious and expensive, should be undertaken Just one such symptom may render a patient ineffectual and miserable, so the fact that the treatment offers two benefits may be the means of getting him to accept and participate in the therapeutic program

URTICARIA

Urticaria is one of the conditions of the skin for which an emotional factor has been noted and accepted for some time As yet it becomes difficult to specify the emotional trends which, among other factors, enter into this condition Stokes, Kulchar and Pillsbury [5] concluded

3 MacKenna, A M B Psychosomatic Factors in Cutaneous Disease, Lancet **2** 679, 1944

4 Wittkower, E Psychological Aspects of Skin Disease, Bull Menninger Clin **11** 148, 1947

5 Stokes, J H , Kulchar, G V , and Pillsbury, D M Effect on the Skin of Emotional and Nervous States Etiological Background of the Urticaria with Special Reference to the Psychoneurogenous Factor, Arch Dermat & Syph **31** 470 (April) 1935

Antimony, as antimony potassium tartrate or stibophen (fuadin®), seems to be outdated in the treatment of granuloma inguinale as a result of the introduction of streptomycin Antimony potassium tartrate is still being used, however, in treatment of cases of mycosis fungoides and pemphigus foliaceus

Intravenous injections of a 10 per cent solution of sodium thiosulfate are sometimes of benefit in the treatment of disseminated neurodermatitis In the treatment of arsenical exfoliative dermatitis, however, that drug has largely been displaced by BAL (2,3-dimercaptopropanol)

Sodium salicylate given by mouth is often effective in treatment of cases of erythema multiforme and erythema nodosum, while phenyl salicylate is more often recommended for urticaria, and salicin for psoriasis Acetylsalicylic acid, alone or in combination with codeine, forms one of the most effective drugs for the relief of pain in herpes zoster

In the treatment of urticaria and other allergic dermatoses the antihistaminic drugs seem to have successfully eliminated all drugs used formerly In the urticaria that results from penicillin, however, epinephrine is often necessary for quick relief and at times ephedrine is also helpful In individual cases benefit may also be obtained after the employment of bile extracts, belladonna tincture, cascara sagrada, magnesia magma, mild mercurous chloride, phenobarbital or calcium gluconate injection

Quinine has been used in the treatment of severe acne vulgaris and resistant cases of lupus erythematosus

Foreign protein therapy, in the form of administration of bactalbumin (aolan®), a solution of peptones and proteoses derived from milk (proteolac®), milk, intravenous injections of typhoid vaccine or autohemotherapy, is often of great value for severe acne vulgaris, neurodermatitis, dermatitis venenata, psoriasis and dermatitis herpetiformis, although for the last-mentioned disorder sulfapyridine has proved to be the most effective drug in cases in which it can be employed

Of the sedatives, phenobarbital is probably the most widely prescribed drug, but at times bromides, chloral hydrate or paraldehyde are more effective when prolonged sedation is desired

Sodium chloride is indicated in the treatment of bromoderma and bromine acne It is effective in the enteric-coated tablets, and it seldom needs to be given intravenously

Vaccine therapy still has its supporters in treatment of recurrent furunculosis and pyodermas, and its employment is not completely outdated by the introduction of penicillin and the sulfonamide compounds Smallpox vaccine is often beneficial in cases of recurrent herpes zoster

since he is too busy looking at his skin and sees little reason why he should shift his attention to his emotions, which he considers as secondary to the state of his skin But as word gets around that one's disposition can be expressing itself in the skin, the physician can obtain more cooperation in the psychotherapeutic treatment

The emotional factor is a variable one, and no one is trying to assert that skin diseases are due to emotions alone But when emotion is a factor, it is one that must be dealt with, if well dealt with, it may be the factor which will give the most practical results in comfort and hence in satisfaction to both patient and physician Dermatologists and psychiatrists must stimulate and help each other to carry on more therapy of the emotional forces which are using the skin for their expression Psychotherapy is not a simple, easily mastered tool, and the patient is not always a willing subject for therapy But, if we try to ascertain what the role of emotions can be in conditions of the skin, we will cure the condition in occasional subjects, improve it in some, make it easier to live with in others and find the specialty of dermatology altogether more interesting through the pleasure which comes from taking a greater interest in human emotions in our daily work as physicians

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(in a dilution of 1 to 16) and a combination of the two are extremely popular In treatment of dermatitis due to plants, solutions of lead acetate (1 teaspoon to 1 quart), potassium permanganate (1 to 5,000) or strong tea generally bring relief In treatment of pyoderma or acute tineal infection of the feet alibour water (water containing zinc and copper sulfate, 1 to 20) or potassium permanganate (1 to 5,000) are of great value Solutions of silver nitrate (1 to 500 or 1 to 1,000) are efficacious in the therapy of acute oozing dermatitis and the weeping streptococcic dermatitis seen on the legs or behind the ears

Of the drying lotions, calamine lotion and starch lotion, with or without the addition of phenol and menthol, are the most widely used When the skin is to be kept from becoming too dry, calamine liniment or lime liniment may be used

Most powders contain starch, boric acid and talc, at times with the addition of other medicaments for specific purposes, such as salicylic acid and thymol in treatment of tineal infections

Soothing ointments include petrolatum, rose water ointment, hydrous wool fat, theobroma oil, lead oleate ointment, zinc oxide ointment and zinc oxide paste

Effective antiperspirants are a 25 per cent solution of aluminum chloride, a 1 per cent solution of formaldehyde and, for the feet, a 1 4,000 solution of potassium permanganate

Mercury is still one of the most efficacious drugs for topical use on the skin Except for the few persons who are sensitive to the drug, ammoniated mercury in the form of a 3 per cent to 10 per cent ointment is probably the most suitable medication for impetigo, ecthyma and other pustular infections of the skin Five per cent ammoniated mercury ointment is often rapidly effective in treatment of infected eczema of the auditory canal, and it is also well tolerated in treatment of impetiginized atopic dermatitis Its use is often beneficial in cases of psoriasis and seborrheic dermatitis One per cent ointment of yellow mercuric oxide is useful in treatment of seborrheic dermatitis of the eyelids, and in therapy of pediculosis of the eyelids it is unexcelled A 1 to 5,000 aqueous solution of mercuric oxycyanide is also an effective and clean treatment for seborrheic dermatitis of the eyelids A 1 to 1,000 solution of mercury bichloride has much support for its use in the treatment of folliculitis and also as an ingredient of scalp lotions

In the treatment of sycosis vulgaris an occasionally more effective antiseptic is quinolor® (chlorohydroxyquinoline) At times, however, its employment is followed by a dermatitis Drugs that are also excellent in the treatment of folliculitis, impetigo, ecthyma and other pyodermas are 1 per cent to 3 per cent ointment of iodochlorohydroxyquinoline (vioform®) and 3 per cent to 10 per cent ointment of bismuth tribromo-

former generations, when nothing was known of the causes of most diseases of the skin, an attempt was made to treat the conditions symptomatically Because of the surface location of cutaneous lesions it was possible for physicians to experiment widely with all possible local medications and, by trial and error over the years, to develop topical therapy that was effective Much of accepted dermatologic therapy is based on this tediously developed but long-established foundation

In modern times, when very little more is known about the causes of most diseases of the skin, the emphasis has been placed on etiology The goal set has been to achieve specific treatment pointed to correcting definite etiologic factors This orientation may in time result in a brilliant solution of many of the baffling dermatologic problems There is the drawback, however, that we may for too long be withholding relief of symptoms and even possible cure by so-called shotgun therapy while we spend precious time in taking careful aim with a precision rifle—a weapon that in many instances may not even be loaded

It has been my impression that with the frequent addition of well publicized new drugs to the dermatologic armamentarium, many old ones have undeservedly been pushed into the background of daily thinking Dermatologists now being trained are often unfamiliar with old drugs that still have merit, and they tend to rely more and more on therapeutic weapons that may prove to be ephemeral With the purpose of emphasizing those drugs that have proved to be effective over the years in the work of successful practitioners, I addressed a letter to two hundred dermatologists of experience, asking them to list drugs of long-established usage that they still prescribe Replies were received from nearly all Most of those questioned were generous in listing the drugs they use most often in their work One dermatologist referred me to the "Pharmacopoeia of the United States" (U S P) and the "National Formulary" (N F) for drugs that still have merit I heartily agree that one may practice in our specialty very competently while limiting himself to drugs listed in those two authoritative books It is, nevertheless, true that in our Academy there are many who do not have in their offices, available for easy reference, the latest edition of either work, nor even that excellent small book, the "Epitome of the Pharmacopoeia of the United States and the National Formulary " I am glad to pass on the suggestion, however, and to recommend the "Epitome," always in the latest edition, as a book that should be accessible on every dermatologist's desk A careful study of its contents is rewarding in calling to attention many official preparations, easily compounded and readily obtained, that are useful in the treatment of many dermatoses Most of these preparations have the added virtue of being relatively inexpensive

Naphthalan and ichthammol (ichthyol®) in 5 to 10 per cent ointments are often helpful in the treatment of many chronic dermatoses

Chrysarobin in a 2 to 10 per cent ointment is useful in the treating of chronic patches of psoriasis and lichen chronicus simplex, while a 4 per cent suspension in chloroform works well in the treatment of chronic paronychia and tineal infections between the toes The drug is sometimes extremely irritating, and it is generally being replaced by anthralin ointment (1/10 to 1 per cent) Other drugs with similar action are pyrogallol, acetpyrogall (triacetyl pyrogallol, lenigallol®), anthrarobin and cignolin

Resorcinol is widely used in combination with sulfur lotions in treatment of acne and also in treatment of seborrheic dermatitis For use on the scalp it is available as resorcinol monoacetate (euresol®)

Salicylic acid is added to many ointments for its keratolytic effect It is an active fungicide, and in benzoic and salicylic acid ointment it probably is still the most effective medication for ringworm infections Thymol may be added (0 25 per cent) to increase the fungicidal activity Fifty per cent salicylic acid in petrolatum has been recommended in the treatment of kerion, but in my experience milder ointments have been as effective Forty per cent salicylic acid plaster is effective in the removal of calluses and corns

Silver compounds are drugs that deserve wider use than they enjoy at present Wet dressings of silver nitrate solution (in a dilution of 1 to 1,000 or 1 to 500) often produce a spectacular drying of acute, weeping streptococcic infections on the legs and behind the ears Ten to 20 per cent solutions are useful for cauterizing fissures, and I have found daily applications of 10 per cent silver nitrate solution extremely helpful in treating ingrown toe nails The granulation tissue is destroyed in these cases and is replaced by a tough crust that resists the pressure of the toe nail In treatment of seborrheic dermatitis of the eyelids a 5 per cent solution of argyrol® (a combination of silver with a protein produced by the electrolysis of serum albumin) dropped into the eye is often helpful Chronic ulcers are effectively treated by the Mikulicz ointment, which contains 1 per cent silver nitrate and 10 per cent Peruvian balsam in petrolatum

Iodine in the form of a 10 per cent ointment in lard in my experience is more efficacious in treatment of ringworm of the scalp than are the newer fatty acids Another old remedy for this disease is a 3 per cent solution of salicylic acid in tincture of iodine In alopecia areata 3 per cent iodine in petroleum benzine has the advantage of staining the skin less than does tincture of iodine or Cutler's fluid (equal parts of liquified phenol tincture of iodine and chloral hydrate) In this disease local applications of phenol, soon removed with alcohol, also act as an adequate irritant

used in the treatment of sarcoid, tuberculosis indurativa, papulonecrotic tuberculid and lupus erythematosus, often producing considerable improvement Injections of solutions of ferric cacodylate or sodium arsenate have been employed in the treatment of pemphigus Acetarsone tablets taken by mouth have at times been effective in the treatment of pemphigus and lichen planus Asiatic pills (composed of arsenic trioxide and black pepper) and potassium arsenite solution, however, have been the most popular forms of administering arsenic by mouth, and they have been used especially in the treatment of lichen planus, dermatitis herpetiformis, neurodermatitis, urticaria papulosa, pompholyx, parapsoriasis and vitiligo In the treatment of psoriasis the use of arsenical drugs should be discouraged, for they need to be administered for too long a time to be devoid of danger It must be remembered, however, that in some persons the use of arsenic compounds for even a short period may be followed by serious sequelae

Iodine in the form of a solution of potassium iodide given by mouth is still an important adjuvant treatment of late syphilis It has also been recommended as an adjuvant to streptomycin in the treatment of tuberculosis It is an excellent remedy in cases of blastomycosis, sporotrichosis, actinomycosis, kerion celsi and other deep fungous infections At times it is effective in the treatment of arthropathic psoriasis or resistant psoriasis, a use which is seldom remembered at present In the form of strong iodine solution U S P or iodoform pills it is helpful at times in treatment of cases of lupus erythematosus Intravenous injections of a solution of sodium iodide often relieve the pain of herpes zoster

Mercurial preparations are seldom used at present in the treatment of syphilis As a therapeutic test in late syphilis, however, the oral administration of mercury and chalk tablets is very useful The oral administration of mercury with chalk or yellow mercurous iodide is often effective in the treatment of juvenile warts and lichen planus, while mild mercurous chloride is an excellent cathartic in the treatment of urticaria and toxic erythema

Bismuth compounds given by intramuscular injection have long been used in the treatment of syphilis While at present displaced by penicillin, they are still being employed in the supplementary chemotherapy of that disease In lupus erythematosus and lichen planus they are often effective, either alone or combined with arsenic as in bismuth arsphenamine sulfonate (bismarsen®)

Gold, in the form of intravenous injections of gold and sodium thiosulfate or other gold compounds, is still probably the most effective drug in the treatment of chronic discoid lupus erythematosus, although the percentage of failures with its use is increasing as the years go by

chloroacetic acid Applications of trichloroacetic acid remove patches of xanthelasma Monochloroacetic acid may be used in destroying seborrheic verrucae After the Sherwell removal of an epithelioma solution of mercuric nitrate or ferric subsulfate solution may be applied

For Vincent's infection of the mouth the administration of penicillin troches is no doubt the most effective local treatment It is a mistake, nevertheless, for one to form the habit of using penicillin routinely in all oral conditions In most of them nothing is accomplished by penicillin that cannot be performed as well and more safely by mild mouth washes, such as sodium bicarbonate, magnesia magma or the N F antiseptic solution As a local astringent a mixture of kino tincture and myrrh tincture has a well founded reputation

Finally, for the treatment of itchy legs nothing brings relief as rapidly as the application of Unna's paste boot

Many additional drugs have been recommended for the treatment of various dermatoses I have excluded them from this listing either because I did not have personal experience with their use or because they duplicated without advantage other drugs that are more readily available in the average pharmacy

COMMENT

I feel certain that the medications listed have found great success in the work of some dermatologists and have been complete failures with others The fault is not entirely with the drug, for each drug is but an inanimate servant, capable only of performing the limited tasks within its scope The selection of the particular drug and the determination of the proper concentration, the ideal vehicle and the best method of application are often the factors that decide the therapeutic results In addition, the unmeasured ingredient of every medication is the attitude of the physician who prescribes it Some dermatologists have the power to inspire confidence and to obtain from the patient full cooperation in the carrying out of carefully outlined instructions For one to tell a patient merely to put on cold wet dressings, for example, is to assume that the descriptive command means to him the same as it does to the physician A patient is more likely to perform his duties correctly if he is permitted to explain to the physician just how he plans to carry out the orders and is then corrected Only by making certain that the patient is going to use the medications as prescribed can one hope to obtain the anticipated results This added point may seem trivial to some, but one may also expect much better results from medication prescribed with an air of confidence than from that given with a skeptical attitude that almost dares the patient to get well

I should not like to be set down as an obstinate reactionary, intolerant of all that is new Certainly the sulfonamide compounds, antibiotics,

Of the endocrine substances thyroid is probably used most often It is especially indicated in the treatment of myxedema and hypothyroid loss of hair, but it is also prescribed for scleroderma, onychodystrophy and, at times, for acne Posterior pituitary injection (pituitrin®), 0 25 cc (obstetric dose) given subcutaneously daily, often relieves the pain in herpes zoster and hastens the involution of the disease

Dilute hydrochloric acid is prescribed in cases of rosacea accompanied with achlorhydria

Iron compounds given by mouth, hematinic tablets and injections of crude liver are often valuable in the treatment of severe acne vulgaris, lupus erythematosus and pemphigus, but in the last-mentioned disease a blood transfusion is probably the most rapid procedure for improving the hematologic status of the patient

Preparations of the vitamin B complex, dried yeast and extract of rice polishings are used in the treatment of glossitis, perlèche, pellagra and rosacea, while vitamin A preparations are often beneficial in treatment of cases of keratosis follicularis, keratosis pilaris, ichthyosis and pityriasis rubra pilaris

DRUGS FOR TOPICAL USE

It is in topical therapy that we dermatologists have our greatest heritage It is in this field also that great skill in therapy can be acquired most rapidly by the intelligent interpretation of experience The surface location of cutaneous lesions, the ease of applying many forms of medication and the ready observation of the effects of local applications make the skin an ideal experimental organ A novice who studies minutely the clinical features of all cutaneous lesions and remembers well how they react to different drugs in various concentrations and in diverse vehicles soon has acquired the therapeutic wisdom of a veteran The careful selection of a few effective drugs and their adaptation to the treatment of various diseases in all stages of activity is much more educational than an aimless but wishful flitting from one proprietary mixture to a later one

In cases of generalized pruritus baths may be used to make a patient more comfortable. Cool colloid baths, prepared with starch, bran or oatmeal, are soothing to an inflamed skin Tar baths are antipruritic and at times are also helpful in treatment of extensive psoriasis Baths containing potassium permanganate are useful in the therapy of widespread pyodermas and of pemphigus

Cold wet dressings are often the most soothing form of treatment in acute inflammations of the skin Skim milk containing boric acid is nearly always well tolerated A saturated aqueous solution of boric acid is effective and inexpensive, while aluminum acetate solution

group of patients to investigate fully the effects of a drug, with the controls essential to an accurate appraisal Many clinical investigators as yet lack the mature judgment needed to temper their enthusiasms and to keep them from being carried away by clinical impressions that may not be lasting In dermatologic therapy too many are attempting to run who have not yet fully mastered the art of walking It may seem antiquated to use old drugs and old fashioned to treat patients with the simple purpose of getting them well as quickly as possible Certainly there is more glamour in being up to the minute with the use of the newest drugs and even ahead of the times in the investigation of drugs for which no specific use has yet been found Most of us dermatologists, in my opinion, are most useful, however, when we devote ourselves wholeheartedly to the career of being healers of the sick It is an old-fashioned role, devoted largely to treating diseases that are not new and most often calling for the employment of drugs that have been tested in the crucible of time It is an honorable career and a satisfying one, a career to which, in our highly scientific age, we particularly need converts.

25 East Washington Street

phenate (xeroform®) Dermatitis from the latter two is uncommon, and their employment generally brings gratifying results With rare exceptions it should not be necessary for one to use preparations of the sulfonamide drugs or penicillin topically in the treatment of cutaneous infections These preparations are seldom as effective topically as the drugs previously mentioned, and their use in this form is hazardous

Sulfur has an old and honored place in dermatologic therapy For seborrheic dermatitis it still is the most effective medication, either alone in a 3 per cent to 5 per cent ointment or with the addition of 1 per cent to 3 per cent salicylic acid In various sulfur lotions, such as white lotion, sulfurated lime solution or Kummerfeld lotion (a compound containing camphor spirit, alcohol, tragacanth, precipitated sulfur and distilled water), it has retained its popularity in the treatment of acne Scabies may still be cured by the application of sulfur in a 3 to 10 per cent ointment A 15 per cent solution of sodium thiosulfate will cure tinea versicolor without any messing The pruritus of dermatitis herpetiformis is often relieved by application of a 2 per cent sulfur ointment In the form of a 30 or 40 per cent sulfur paste, sulfur is frequently beneficial in the therapy of seborrheic dermatitis, dermatitis herpetiformis, chronic eczema and other chronic dermatoses

Tar is a remedy of great value for many dermatoses In nummular eczema and infantile eczema coal tar ointment generally produces rapid improvement, and in eczema of the nipple the response is excellent Tar ointments are beneficial in treatment of tineal infection of the hands and feet and at times also in that of psoriasis and recalcitrant eruption Solutions of crude coal tar in acetone, chloroform or collodion are much cleaner to apply but are not as effective as the ointment form The various distilled or decolorized tars are also much less effective than crude coal tar, but distarol® and zetar® are comparatively good clean substitutes The wood tars (pine tar, juniper tar and rectified oil of birch tar) should be used only in chronic dermatoses, for their employment in more acute stages generally increases the inflammation "Oil of cadeberry"[1] has all the benefits of juniper tar, but it has a much more pleasant odor In treatment of resistant patches of psoriasis or lichen chronicus simplex, tar-containing ointments, such as compound ointment of sulfur or Dreuw's ointment (a preparation containing salicylic acid, chrysarobin, rectified oil of birch tar, medicinal soft soap and petrolatum) may be used Tar should never be used in any form in the presence of furuncles or other pustular infections, for fear of the production of lymphangitis Folliculitis from the use of tar can generally be prevented by removal with a bland oil of all the old residue on the skin before a new application is made

1 A product of Muth Bros & Co, Baltimore, containing barbados tar and oil of juniper berry

In 1946, Rowe [4] reported a series of 80 patients (42 per cent of 182 patients with eruptions of the hands) with "atopic dermatitis of the hands" due to food allergy, and concluded from his observations that "dermatitis of the hands in the average population may result more frequently from atopic allergy to food than from any other cause"

At about the same time, Flood and Perry [5] reported two series of patients, 30 patients with "recurrent, vesicular eruptions of the hands" being discussed in one paper,[5a] and 13 patients with "eczematoid dermatitis" in the other,[5b] with food sensitivity comprising the primary etiologic factor Flood and Perry did not attempt to estimate the exact incidence of food allergy as the predominant factor in such eruptions, nor did they compare its importance with other factors, but they implied that specific sensitivity to foods is at least as important as any other etiologic factor

Our experience in the study and treatment of eczematous dermatitis of the hands, feet and other sites is recorded in this paper with an attempt at a critical evaluation of the relative importance of specific food sensitivity as a primary or contributory etiologic factor in such eruptions One of us (C S L) had an opportunity to accumulate considerable experience in this therapeutic approach during World War II, but none of the patients encountered at that time is included in this report because adequate follow-up was not possible All the patients in this series were seen and followed in our joint private practice We have included only those patients with an adequate period of follow-up observation and in whom a predominant role of food allergy in the eruption seemed inescapable Furthermore, we have not included patients from whom complete cooperation was not obtained This fact has limited the number of patients in our series, but it is believed that the experience with this group is representative and the major aspects of this subject are illustrated in the case material It is believed that one reason for some difference of opinion in regard to the importance of the food allergy factor in eczematous dermatitis is the failure to realize that food sensitivity is only one of the etiologic agents in many of these cases and that the complete cure and, indeed, recognition of a contributory food allergy factor depend on the identification and adequate management of all the factors concerned in the individual case This principle is well illustrated in many of our cases

It is essential to attempt to clarify the descriptive terms applied to this group of eczematous eruptions because nomenclature is cumbersome

4 Rowe, A H Atopic Dermatitis of the Hands Due to Food Allergy, Arch Dermat & Syph **54** 683 (Dec) 1946

5 (*a*) Flood, J M, and Perry, D J Recurrent Vesicular Eruptions of the Hands Due to Food Allergy, J Invest Dermat **7**·309, 1946, (*b*) The Role of Food Allergy in Eczematoid Dermatitis, Arch Dermat & Syph **55**.493 (April) 1947

Copper in the form of a 10 per cent ointment of copper oleate is therapeutically active in ringworm of the scalp, and alibour water (1 to 20) is an excellent wet dressing for Bockhardt's impetigo and other infected lesions

It is possible that hexachlorocyclohexane in a vanishing cream base (kwell® ointment) will replace all other antiparasitic drugs Until its place has been firmly established and its possible dangers are fully understood, it is well to remember that other good remedies for scabies include sulfur, Peruvian balsam and its derivative, benzyl benzoate, betanaphthol, and storax

Benzoin tincture is often applied to fissures A 50 per cent ointment of benzoin tincture is an excellent remedy for chronic ulcers, as is the application of Aloe vera leaf or ointment Urea solution is useful in removing necrotic tissue from ulcers Cod liver oil ointments are efficacious in the treatment of chronic ulcers and of burns, and for burns trinitrophenol solution is rapidly effective in treatment of patients who can tolerate it

Of the various dyes used for topical application, Castellani's paint (a preparation containing basic fuchsin, phenol, boric acid, acetone and resorcinol) is by far the most valuable in the treatment of tineal infections on moist areas It is best to begin by using a 25 per cent strength paint and then to strengthen it gradually A 1 per cent solution of methylrosaniline chloride is excellent in treatment of yeast infections, especially those on the webs of the fingers and in the folds of the skin and paronychia A 5 per cent solution of methylrosaniline chloride in 20 per cent alcohol is effective in the prevention of infection at the site of removal of warts or moles Five per cent scarlet red ointment is an old and effective remedy for chronic ulcers

For screening agents in lupus erythematosus and sensitivity to light, preparations of phenyl salicylate, quinine or tannic acid are satisfactory and are less likely to produce dermatitis than sodium para-aminobenzoate (Paba®) cream

The application of 10 per cent bergamot oil in alcohol followed by exposure to the ultraviolet rays at times hastens the return of pigment in patches of vitiligo

Five per cent ethyl aminobenzoate (benzocaine®) in flexible collodion applied to insect bites relieves the pruritus in many cases

Condyloma acuminatum is best treated by the application of 25 per cent podophyllum resin in alcohol One must exercise great care not to treat too large an area at one time, for fear of producing severe inflammation

Verrucae under the nails or about the nails may be treated by applying 4 per cent formaldehyde solution, sulfurated lime solution or mono-

It is realized that there are other possible contributory factors, such as physical allergies, diseases of the gastrointestinal tract, liver or kidney, intercurrent infections of various types and metabolic disturbances

METHOD OF STUDY

It is our practice to consider specific food sensitivity as a possible primary or contributory factor in all cases of eczematous dermatitis, regardless of the site of involvement, unless it is obvious on initial examination or a brief subsequent period of observation that other causes are responsible

The methods of study in regard to a possible food allergy factor which we have used include one or more of the following regimens

(1) A strict trial diet (as outlined by Flood and Perry,[5]) which is feasible only for hospitalized patients

(2) A so-called basic "nonallergenic diet," consisting of beef, lamb, chicken, canned pears, canned apricots, prunes, baked or boiled potatoes, lettuce, celery, string beans, red beets, lima beans, weak tea, sugar, salt, white vinegar, ry-krisp® or pure rye bread, peach preserves and apple jelly, followed by addition of foods one at a time at five-day intervals after a base line of improvement has been established

(Recently, following the suggestions of Winston and Sutton,[6] we have added only one food at each meal [For example, on the first day of the diet, the menu is as follows Breakfast canned pears, luncheon—canned pears and tea with sugar, and dinner canned pears, tea with sugar and lamb On subsequent days other foods of the basic diet are added in a similar manner] If pruritus and/or new lesions of any type are noted after the addition of a new food, all new foods which have been added in the previous twelve-hour period are eliminated from the diet)

(3) A minimal elimination diet ("spot" elimination diet), interdicting sea foods, chocolate, nuts, citrus fruits, tomatoes, pork, cheese and coffee

(4) A diet diary

It must be realized that considerable individualization is necessary, inasmuch as there are practical limitations in the study and treatment of patients from the standpoint of food allergy A high percentage of patients do not like strict diets, hospitalization is not available or feasible for everyone, and, on an outpatient basis, business and social responsibilities make it difficult for persons to follow even simple elimination diets There are very few patients who find it possible to eat all their meals at home, and, if they do, the necessity of special cooking for one member of the family is a complicating factor Furthermore, the vast majority of patients are not easily convinced that food allergy may constitute a factor in their particular case Only a small number of our patients will follow diets as limited as the Rowe elimination diet [6] or the so-called "basic nonallergenic" diet for more than two

6 Winston, B H, and Sutton, R L, Jr Dermatitis of the Hands Due to Ingested Allergens, Arch Dermat & Syph **58** 335 (Sept) 1948

antihistaminic agents and other new drugs have opened new roads to hope in the treatment of many diseases hitherto serious in their prognosis In many instances more progress can be made in hours with the use of new drugs than was possible in months with old-fashioned treatment The risk of sensitization and toxicity inherent in many of these drugs makes it prudent, however, that they be used only when they are needed Not only dermatologists, but also physicians lacking dermatologic training, have tended too much in recent years to try these new drugs as the first medication in the treatment of all dermatoses before turning to older drugs that have proved adequate Furthermore, because of the vital importance of sulfonamide compounds and antibiotics in the treatment of dangerous infectious diseases, it is imperative that these drugs be reserved, if possible, for exigencies when they are desperately needed We dermatologists are seldom called on to treat diseases so serious as to warrant the risk of exhausting a patient's capacity for using a drug that might in the future prove to be life saving

A dissertation on good dermatologic therapy utilizing well established drugs would be incomplete if it failed to stress the most important requisites for obtaining good therapeutic results, namely the correct diagnosis of the disease and the proper appraisal of the stage of activity present One must recognize, for example, not merely that he is dealing with a tineal infection of the feet before instituting proper treatment, it is just as important for one to ascertain whether therapy should be actively fungicidal, in the chronic stage of the disease, or merely soothing, when the skin is acutely inflamed It is important for the physician to recognize the clinical picture of overtreatment dermatitis that may be masking the features of the original dermatosis Discontinuing all previous medication in such cases and the cautious use of soothing treatment will often give the patient great relief and may also bring to light the diagnostic features present One should, in addition, always keep in mind that he is treating a patient with a cutaneous disorder rather than merely treating a cutaneous disease All of us need constant reminding that the skin is often a window to internal disease A dermatologist's diagnostic eye and therapeutic acumen should encompass not only the skin but also the patient living within it

Finally, a clinical dermatologist's chief function (and most of us are primarily clinicians) is to bring to his patients relief from suffering To this end he should utilize all measures of established merit that apply to each case For this vocation most of us are well trained It has become popular in recent years, however, for many dermatologists to become clinical investigators for every new drug and proprietary mixture that is brought to market For this highly critical function most of us are not adequately equipped Not many have a large enough

REPORT OF CASES

CASE 1.—M. C., a housewife aged 32, was seen because of a patchy, eczematous dermatitis of twenty years' duration, involving the hands and the left lower eyelid, the eyelid having become involved only within the past four months. The eruption was characterized by erythematous, scaling, oozing, rather well demarcated, vesicular plaques on the right palm and on all surfaces of the right third finger, as well as on the sides and dorsal surface of the second and fifth fingers of the left hand. The patient had severe pruritus, which had interfered with sleep and other activities. Several weeks after she came under our observation, she also had a brief episode of an oozing, pruritic, intertriginous dermatitis of the axilla and groins. At various times vesicopustules and residual pyogenic crusts were noted as a part of the process. This patient had not been completely free of lesions since the onset, although there had been many exacerbations and partial remissions. The longest and most significant partial remission had occurred approximately two years before her first visit, during the time that she was on a reducing diet consisting of grapefruit juice, eggs, toast, cheese, tea, lettuce and tomatoes. On several occasions during the past three years, she had had attacks of intertriginous dermatitis in the axilla and groins persisting for two to three weeks, followed by a complete remission.

The patient had been treated by at least twelve different physicians, including five dermatologists, who had given her a total of approximately twenty-five roentgen ray treatments, and she had been informed by one of her physicians that he had given her as much roentgen therapy as her hands would tolerate. The use of numerous ointments and other types of local treatment, as well as the employment of a soap substitute and strict avoidance of soap and water and all household contactants, had had no apparent effect on the course of her lesions.

There was a history of infantile eczema in early infancy and of relatively transient attacks of acute urticaria in childhood. The familial allergic history was noncontributory except that the patient's sister had had apparent hydrorrhea due to vasomotor neurosis (vasomotor rhinitis) and urticaria.

The management and course of this patient's eczematous dermatitis during the eighteen months of observation were as follows:

1. Patch tests with numerous household contactants, cosmetics and routine test materials had negative results except for 1 plus reactions to dilutions of 1: 1,000 of bichloride of mercury, prell® shampoo, lustre creme® shampoo, rinso® and resorcin, although all these reactions were minimal.

2. Initially, on an outpatient basis, the patient was placed on a diet of baked potato, beef, lamb, string beans, carrots, tea, sugar, grapefruit juice, boiled eggs, canned pears, prunes, canned apricots, lettuce and tomatoes. In addition, she was asked to avoid prell® shampoo, lustre creme® shampoo, and rinso®. Local treatment consisted of potassium permanganate soaks and 3 per cent ichthammol (ichthyol®) in zinc oxide ointment. Housework of all types was reduced to a minimum by the patient's employing a full time maid and enlisting the cooperation of her husband for dishwashing when the maid was not available. She did not have significant, sustained improvement on this regimen of treatment.

3. Therefore, she was hospitalized for a period of two weeks. She was placed on a strict trial diet (Flood and Perry), with sugar water during the first twenty-four hours, baked potato during the next twenty-four hours and lamb during the next twenty-four hours, during this time there was pronounced continued improvement, with almost complete disappearance of pruritus after the first forty-eight hours. Tea was added on the fourth day, and eight hours after the first cup of tea,

SPECIFIC SENSITIVITY TO FOODS AS A FACTOR IN VARIOUS TYPES OF ECZEMATOUS DERMATITIS

CLARENCE S LIVINGOOD, M D
GALVESTON, TEXAS
AND
DONALD M PILLSBURY, M D
PHILADELPHIA

MANY observers[1] have reported cases of chronic, recurrent, vesicular eruptions of the hands due to various food allergens Other authors,[2] who have written on the problem of eczematous dermatitis of the hands, designated by various terms such as "chronic eczematoid dermatitis of the hands" and "recurrent vesicular eruptions of the hands," have listed food allergy as one of the infrequent and relatively unimportant etiologic factors Stokes,[3] in particular, emphasized the concept that such eruptions of the hands, as well as chronic eczematous dermatitis at other sites, are often due to multiple etiologic factors He stressed the importance of a "factorial analysis" in the study of such patients and included food allergy among the various etiologic considerations

Read at the Sixty-Eighth Annual Meeting of the American Dermatological Association, Inc, San Diego, Calif, April 27, 1948

From the Department of Dermatology and Syphilology, Graduate School of Medicine, University of Pennsylvania, Dr Donald M Pillsbury, Director

For many of these patients, scratch, intradermal and patch tests were done by Dr Norman R Ingraham Jr Our associate, Dr Malcolm C Spencer, assisted in the management of some of the patients included in this series

1 Buckley, L D Diet and Hygiene in Diseases of the Skin, J A M A **59** 535 (Aug 17) 1912 Wise, F, and Wolf, J Dermatophytosis and Dermatophytids, with Particular Reference to Differential Diagnosis of Dyshidrosiform Eruptions of Hands and Feet, Arch Dermat & Syph **34** 1 (July) 1936 Wise, F, in discussion on Lehmann, C F Acute Vesicular Eruptions of the Hands and Feet, ibid **21** 499 (March) 1930 Engman, M F, Jr, in discussion on Andrews, G C, Berkman, F W, and Kelly, R J Recalcitrant Pustular Eruptions of Palms and Soles, ibid **29** 548 (April) 1934

2 Lane, C G, Rockwood, E M, Sawyer, C S, and Blank, I H Dermatoses of the Hands, J A M A **128** 987 (Aug 4) 1945 Callaway, J L, and Barefoot, S W The Diagnosis and Management of Chronic Eczematoid Dermatitis of the Hands, North Carolina M J **1** 547, 1940

3 Stokes, J L, Lee, W E, and Johnson, H M Contact, Contact-Infective and Infective Allergic Dermatitis of the Hands, with Especial Reference to Rubber Glove Dermatitis, J A M A **123** 195 (Sept 25) 1943

15	56	F	Secretary	1 mo	1 yr	Hands, forearms, neck, right upper eyelid	Basic "nonallergenic" diet, diet diary	1 Food allergy	Oranges, grapefruit, wheat, coffee(?), eggs(?), pineapple(?)	Prominent psychogenic factor
16	56	F	Secretary	10 yr	6 mo	Right upper eyelid, right postauricular area	Spot elimination diet, diet diary	1 Food allergy	Chocolate, lobster, clams, crab	Exacerbations following ingestion of food, accompanied with nausea and gastrointestinal pain
17	22	F	Salesgirl	11 yr	8 mo	Hands	Scratch test-negative diet, diet diary	1 Food allergy	Cheese, pimento, pork pecans	The only patient in our series for whom a scratch test-negative diet was successful, happened to result in the elimination of all causative foods
18	12	M	Student	3 mo	1 yr	Posterior surface of neck	Spot elimination diet, diet diary	1 Food allergy	Chocolate	Repeated exacerbations on addition of chocolate to diet, after six months patient able to eat chocolate occasionally without exacerbation
19	52	M	Executive	6 mo	8 mo	Hands	Basic elimination diet, diet diary	1 Food allergy 2 Pyogenic infection	Rice	Clearing of bacterial infection along with improvement of dermatitis, without specific antibacterial therapy
20	21	F	Secretary	15 mo	6 mo	Hands, right cheek	Basic elimination diet, diet diary	1 Food allergy	Milk, wheat	Repeated sharp exacerbations on addition of milk or wheat products to the diet
21	40	M	Clerk	4 yr	6 mo	Hands	Hospitalization, strict trial diet, diet diary	1 Food allergy 2 Pyogenic infection and pyogenic sensitization	Chocolate, peanut butter	Incomplete clearing until pyogenic factor had been treated with parenterally administered penicillin and fever therapy
22	39	F	Housewife	4 yr	2 yr	Hands, feet	Hospitalization, strict trial diet, diet diary	1 Food allergy 2 Pyogenic infection and pyogenic sensitization 3 Contactant	Pepper, cinnamon, chicken, bacon, smoked ham, onions, paprika	Persistence of sensitivity to causative foods for as long as eighteen months after clearing of eruption
23	28	F	Secretary	3 yr	1 yr	Face	Hospitalization, strict trial diet, diet diary	1 Food allergy 2 Drug	Rice, butter, sweet potatoes, carrots, tomatoes, oranges, eggs, chocolate	Eczematous and folliculopustular lesions, repeated exacerbations after ingestion of vitamin B complex capsules
24	20	F	Nurse	2½ yr	2 yr	Left axilla	Hospitalization, strict trial diet, diet diary	1 Food allergy 2 Contactant	Oranges, grapefruit	Eruption resembling a fixed drug eruption
25	12	M	Physician	3½ yr	6 mo	Hands	Hospitalization, strict trial diet, diet diary	1 Food allergy 2 Contactant 3 Drug	Tomatoes, oranges, grapefruit	Phenobarbital, both as contactant and ingestant, one of the etiologic factors
26	28	M	Foundry worker	3 yr	9 mo	Hands, ankles	Hospitalization, strict trial diet, diet diary	1 Food allergy	Pork, milk, potatoes	Onset of dermatitis, on the dorsal surface of the hands, as a contact dermatitis due to a primary irritant, persistence for years (five) and complete disappearance on elimination of causative foods, repeated exacerbations demonstrated on addition of responsible foods, flare ups within fifteen to thirty minutes after ingestion of causative food

and confusing, especially for the physician who is not a dermatologist The same type of disease process has been referred to by various authors as eczema (with numerous qualifying terms such as vesicular and nummular), eczematoid dermatitis of the hands and feet, chronic, vesicular eruptions of the hands, "atopic dermatitis of the hands" and "eczematous contact-type allergic dermatitis," among other terms It would be desirable to use terms based entirely on etiology, but this is not possible because the cause in many cases is unknown, in other instances the etiologic agents are multiple, and they may vary from time to time in the same patient Therefore, any classification must be partly etiologic and partly morphologic There is general agreement in the use of the following terms (or various synonyms), either because the dermatitis is due to a single etiologic factor or because of the characteristic type, distribution and course of the cutaneous eruption (1) contact dermatitis, (2) dermatitis medicamentosa (eruptions due to drugs), (3) atopic dermatitis, (4) infantile eczema of atopic type, (5) seborrheic dermatitis and (6) lichen simplex chronicus

We use the term eczematous dermatitis as a morphologic diagnostic term for all other types of chronic and recurrent dermatitis due to a wide variety of external and internal causes or of unknown etiology It is the group of cases in this category which has been responsible for most of the confusing synonyms The individual entities within the syndrome are often not sharply defined, and transitional types are encountered For example, it may be difficult to determine whether the patient has a contact dermatitis with secondary bacterial infection, or a pyoderma with secondary eczematous changes due to sensitization to bacteria, or reactions to local treatment

The cataloging of the individual patient into a distinct diagnostic category depends on qualification of the term by adding the site or sites of involvement and the etiologic factors, if they are determined and proved (so far as doing so is possible) The following etiologic factors are variously recognizable in (chronic) eczematous dermatitis

1 Allergic contactant } (Dermatitis in which these factors are the only factors
2 Primary irritant } is classified under the heading of contact dermatitis)

3 Food allergy

4 Secondary bacterial invasion and sensitization (Impetigo and other primary uncomplicated pyogenic infections of the skin are not included)

5 Drug allergy (If this is the only factor the condition should be included under the heading of dermatitis medicamentosa)

6 Pollen and inhalant allergy

7 Mycotic infection and mycotic sensitization (Uncomplicated primary fungous infection and dermatophytids are classified as such)

8 Psychosomatic, traumatic, thermal, endocrine, peripheral, vascular and dyshydrotic factors and foci of infection

9 Undetermined etiologic factors

CASE 2—B M, a nurse aged 29, had first noted approximately one year previously what was described as a pruritic, vesicular patch of dermatitis on the dorsal surface of her left hand It had occurred approximately ten hours after she had mixed penicillin solution, during which procedure a moderate amount of the concentrated solution had come into contact with the affected site During the next three months she had had several recurrences of pruritic, vesicular dermatitis on the dorsal surface of the hand, with complete remission between these episodes After this period, she had had more frequent attacks, as well as extension of involvement to the dorsal surface and sides of several fingers Furthermore, the lesions persisted between attacks, and at times superficial fissuring, which interfered with the movement of her fingers, occurred

Six months after the initial onset, all lesions cleared up completely during a three weeks' vacation, when the patient was away from her work as a clinic nurse There was prompt recurrence when she returned to work At this time she consulted a dermatologist, who found positive reactions to patch tests with penicillin, contact with this drug was discontinued There was slight improvement, but complete clearing did not occur, and the patient continued to have periodic exacer-

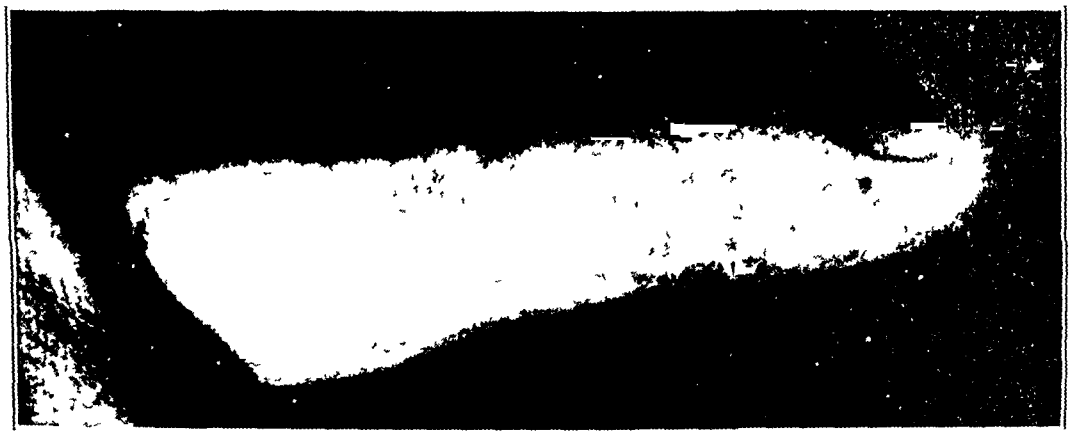


FIG 1 (case 2) —One of the eczematous plaques on the fingers, which on one occasion flared up simultaneously with the exacerbation of a lesion on the eyelid

bations Patch-testing was then done with procaine hydrochloride (novocain®) and streptomycin, with positive results, and therefore contact with these drugs was discontinued However, despite this action, during the next three months the patient continued to have repeated flare-ups, and finally it was necessary for her to discontinue her work for the second time Within one week, there was significant improvement, but she continued to have new vesicles and also had one distinct, rather severe exacerbation which was certainly not related to contact with penicillin, procaine hydrochloride or streptomycin At the time of the exacerbation she consulted an allergist, who confirmed the previously reported positive reactions to patch tests and also demonstrated that she had pronounced sensitivity to trichophytin, for this reason he advised a series of injections with trichophytin as an attempt at desensitization Because of financial reasons, it was essential for her to return to work There was no improvement, and indeed the severity and extent of her lesions gradually increased during the next two months, the exacerbations were not related to the injections of trichophytin

Other treatment included strict avoidance of soap and water, with use of a soap substitute, superficial roentgen therapy and application of several unidentified ointments

weeks, and, if there is no significant improvement at the end of that time, there is difficulty in persuading the patient to continue any type of dietary restriction

The evaluation of the course of the eruption is complicated by the fact that the interval between the ingestion of food and the beginning of the exacerbation varies in different patients Furthermore, there is an important quantitative factor, and, in addition, the presence of concomitant pyogenic and pyogenic sensitization, allergic contactant or other factors interferes with the interpretation of results

It was shown by many investigators [7] that limitation of the diet on the basis of scratch tests to food is rarely helpful, and our experience is in agreement with this conclusion However, many patients who do not like dietary restrictions in principle will cheerfully adhere to a restricted diet based on the results of scratch tests, often for years

Because of all these limitations, we have been obliged to use various methods of approach, including the strict trial diet as outlined by Flood and Perry, a basic nonallergenic diet which follows the general principles of the Rowe elimination diets and a "spot" elimination diet from which foods with a high allergenic index are eliminated All the patients who were studied by means of the strict trial diet were hospitalized After hospitalization, during which pronounced improvement or complete cure was affected in all patients in whom food allergy was an important etiologic factor, new foods were added at five day intervals Diet diaries were used in all cases because, for one thing, they assist patients in learning to recognize their exacerbations and to correlate them with the addition of possible causative foods

PRESENTATION OF CASES

We have been able to demonstrate either a primary etiologic or an important contributory etiologic food factor in a total of 26 patients who have had adequate follow-up observation For an additional 41 patients, specific sensitivity to food was an apparent important component of the dermatitis, but we were not able to establish unequivocal proof of this fact, or the observation period was not sufficient at the time of writing, and, therefore, their cases are not included in the series which constitutes the basis for our discussion

Lack of space makes it impossible for us to include the individual case histories of all these 26 patients Therefore, only 3 representative cases are presented in detail, pertinent data on all the 26 patients are summarized in the accompanying table

7 (*a*) Winston and Sutton [6] (*b*) Rowe, A H Elimination Diet and the Patient's Allergies A Handbook of Allergy, ed 2, Philadelphia, Lea & Febiger, 1944

a summary of which follows Reactions to patch tests were negative for a long list of household and other contactants except for crystalline penicillin G (1 cc containing 25,000 units), 3 plus, a 2 per cent aqueous solution of procaine hydrochloride, 3 plus, and o'cedar® furniture polish (50 per cent in olive oil), 3 plus Scratch and intradermal tests with aqueous protein extracts of common dust-borne allergens, except for those with mixed feathers, sheep dander, rabbit hair and cow dander, had negative reactions Scratch tests with 140 foods had negative results except for weakly to moderately positive reactions to almonds, bananas, lima beans, Roquefort cheese, cherry, chicory, cinnamon, coconut, dates, grapefruit, milk, mustard, onions and poppy seed

2 She had about a 50 per cent improvement during the three week period when she was away from work, but she continued to have exacerbations characterized by intense pruritus and the appearance of new vesicles, particularly at the periphery of the involved sites At times, the eyelid lesion flared up concomitantly with the



Fig 3 (case 22) —This site of involvement had flare-ups on numerous occasions when one of the responsible food allergens was added to the diet The lesions on the patient's hand are illustrated in figure 2

lesions on her hands, but at other times either the eyelid lesion or the hand lesions flared up independently The only local treatment which was used consisted of aluminum acetate solution (1 20) soaks several times daily, followed by application of 3 per cent itchthammol in zinc oxide ointment After the allergy work-up, o'cedar® furniture polish was added to the list of contactants for her to avoid, and also the patient was asked to follow a diet consisting of only the foods which gave entirely negative reactions on scratch tests She returned to work, inasmuch as the severity of the exacerbations and their frequency during the time when she was away from work were such that the financial sacrifice did not seem justifiable

3 There was no significant improvement on a scratch test–negative diet during the next three week period, and therefore chocolate, coffee, orange, cheese and tomato and nuts were also eliminated from the diet, in addition, the patient was asked to keep a careful diet diary Wheat and eggs were not added to the list

Data Concerning Twenty-Six Patients with Eczematous Dermatitis

Case No	Age	Sex	Occupation	Duration	Period of Observation	Sites of Involvement	Methods of Study	Factors	Foods Which Caused Exacerbation	Comment
1	32	F	Housewife	20 yr	18 mo	Hands, left lower eyelid, axillas, groins	Hospitalization, strict trial diet, diet diary	1 Food allergy 2 Pyogenic infection and pyogenic sensitization	Tea, apricots, broccoli, cauliflower, cabbage, peaches	Pyogenic factor treated with penicillin administered parenterally
2	29	F	Nurse and housewife	1 yr	6 mo	Hands, left lower eyelid	Basic "nonallergenic" diet, diet diary	1 Food allergy 2 Contactant	Eggs, milk	Onset as contact dermatitis
3	30	F	Secretary	15 mo	1 yr	Feet, hands	Basic "nonallergenic" diet, diet diary	1 Food allergy	Wheat, chocolate, coffee, shrimp, crab, lobster	Scratch test-negative diet partially successful
4	28	M	Mail carrier	4½ yr	9 mo	Hands	Hospitalization, strict trial diet, diet diary	1 Food allergy 2 Pyogenic infection and pyogenic sensitization	Milk, chocolate, pork, tomatoes	Pyogenic factor treated with parenterally administered penicillin combined with fever therapy
5	44	M	School teacher	1 yr	3 mo	Perianal region, scrotum, hands	Spot elimination diet, diet diary	1 Food allergy	Chocolate, shad, shrimp	No resemblance of scrotal dermatitis to lichen simplex chronicus
6	30	F	Secretary and housewife	6 mo	4 mo	Hands	Basic "nonallergenic" diet, diet diary	1 Food allergy	Cinnamon, onions, eggs, smoked ham	
7	55	F	Housewife	6 mo	2 yr	Hands	Spot elimination diet, diet diary	1 Food allergy 2 Contactant	Nuts, grapefruit, oranges	Prominent psychogenic factor
8	27	M	Medical student	2 mo	16 mo	Hands	Hospitalization, strict trial diet, diet diary	1 Food allergy 2 Contactant 3 Drug	Wheat, milk, pork(?), chicken(?), carrots(?)	Exacerbations with use of naphazoline ("privine") nose drops, patient not cured until smoking was discontinued, positive reaction to patch test with tobacco
9	67	M	Civil engineer	1 yr	17 mo	Legs, ankles, thighs, hands, left upper and lower eyelids	Basic "nonallergenic" diet, diet diary	1 Food allergy	Wheat, veal, rye	No improvement until responsible foods were discontinued for several weeks—which observation is unusual
10	37	F	Housewife	6 yr	20 mo	Hands	Hospitalization, strict trial diet, diet diary	1 Food allergy 2 Pyogenic infection and pyogenic sensitization 3 Drug	Broccoli, string beans, lima beans, vanilla, peas, sweet corn	Exacerbation on ingestion of sulfadiazine and pentobarbital sodium, acetylsalicylic acid, pyogenic factor treated with penicillin given parenterally
11	31	F	Housewife	4 mo	9 mo	Hands, legs	Basic "nonallergenic" diet, diet diary	1 Food allergy	Wheat, chocolate peaches(?), pork(?)	Unusually severe, extensive involvement, with rapid improvement on management on an outpatient basis
12	30	F	Secretary	5 mo	18 mo	Hands	Spot elimination diet, diet diary	1 Food allergy	Grapefruit, peanuts, oranges	Prominent psychogenic factor
13	4	M	Preschool child	1 yr	6 mo	Buttocks, legs	Basic "nonallergenic" diet, diet diary	1 Food allergy	Eggs, chocolate, pork	Exacerbations on numerous attempts to add causative foods to diet
14	50	M	Executive	1 yr	1 yr	Hands, legs	Hospitalization, strict trial diet, diet diary	1 Food allergy	Almonds, tomatoes, pork, Scotch whisky, oranges(?)	Patient completely incapacitated by his dermatitis

flare-up ensued within a short time after the ingestion of only one egg, six weeks after the lesions had become quiescent, a flare-up did not occur until the patient had eaten one egg daily for six consecutive days, several months later, she was able to eat three eggs weekly, as well as foods containing eggs, without any return of pruritus or objective signs This spontaneous desensitization is a common sequence of events, provided that all causes of the eczematous dermatitis have been eliminated and the lesions have remained entirely clear for several weeks to several months It may be noted that she had a negative reaction to a scratch test with the only significant food allergen which was one of the proved causative factors



Fig 4 (case 11) —The patient also had large, oozing, eczematous plaques on both legs Numerous exacerbations such as the one illustrated were demonstrated on the addition of wheat and chocolate to the diet

Case 3 —H H , a secretary aged 36, was referred to us because of an unusually severe, patchy, eczematous dermatitis of the feet and hands, with maximal involvement of the feet, which had been present for fifteen months This was characterized by scaling, erythematous, superficially denuded, crusted, vesicular, fissured plaques on the inner surface of the right foot, extending from the instep to the dorsal surface of the foot and involving part of the ankle, the dorsal surface of the right foot at the base of the first interdigital space and extending into the interdigital space, the instep of the left foot and the medial surface of the left foot just above the heel The borders of the lesions were not well demarcated, only a few vesicles were seen In addition, there was a faintly erythematous, rather well demarcated, dry, slightly lichenified plaque on each palm, as well as a few superficial vesicles along the sides of several fingers All lesions tended to be dry, scaly and somewhat lichenified rather than oozing, although there was some exudation at several sites on the feet

an interval during which the patient had had 3 cups, there was a sharp, distinct, relatively severe exacerbation, characterized by intense pruritus and recurrence of erythema, vesiculation and oozing Within a brief period evidence of secondary bacterial infection was noted After this episode, 50,000 units of penicillin every three hours was administered for five days, during which time there was a slow but continued improvement At the end of two weeks of hospitalization, the eczematous dermatitis was less active than at any other time since the patient had come under our observation There were no vesicles or pustules, and the pruritus had almost disappeared However, there was some residual scaling, erythema and superficial fissuring The patient was discharged from the hospital, with instructions to follow a diet consisting only of baked potato, lamb and string beans

4 Continued improvement was noted during the next seven weeks except for significant exacerbations following the trial addition of tea and dried apricots to the patient's diet During this time, the diet had been increased to include beef, lamb, string beans, sugar, chicken, turkey, lettuce, asparagus, carrots, baked potatoes, canned pears, prunes, apples, eggs, white bread, saltines, vanilla ice cream, milk and ginger ale All these foods had been added gradually, one at a time, with approximately two to three days between each addition No attempt was made to add further foods during the next month, and during this time the lesions on the hands and eyelids cleared up completely

5 In the next six weeks, in the same manner, the patient added cottage cheese, American cheese, almonds, corned beef, bananas and cherry gelatin, without any exacerbations During this same period she had prompt exacerbations manifested by pruritus, erythema and a few tiny vesicles at previously involved sites, four hours after the addition of broccoli and cauliflower to her diet on two separate occasions

6 During the next six weeks the patient continued to remain free of any signs of involvement except for a slight exacerbation twelve hours after the addition of cabbage and canned peaches to her diet on two separate occasions In the meantime she had added celery, onions, green pepper, mushrooms, beets, mashed turnips, beef and calf liver and several types of fish, so that at this time the only foods restricted from her diet were tea, dried apricots, broccoli, peaches, cauliflower and cabbage

7 During the past year she has been free of involvement and has been able to do all her own housework with no effort to protect her hands from excessive contact with soap and water and other cleansing agents

It is interesting to note that tea has been the main beverage of this patient throughout her adult life because she does not like coffee and, furthermore, that she has always eaten dried apricots

The diagnosis was eczematous dermatitis of the hands, left lower eyelid, axilla and groins, with food allergy (tea, apricots, broccoli, cauliflower, cabbage, and peaches), pyogenic infection and pyogenic sensitization as factors

Comment This is an example of a difficult food allergy problem It is probable that this patient would have been included in the group of those in whom treatment was a failure or, rather, that the food allergy factor would not have been recognizable if it had not been possible for her to be hospitalized and if her cooperation had not been unusually good It may be noted that this patient reacted to several members of the cabbage family, as well as to related fruits *She is the only patient* in our entire series for whom tea was recognized as a food allergen

ichthammol in zinc ointment was prescribed A summary of an allergy work-up, done by Dr Norman Ingraham Jr, follows

A Patch tests of a wide variety of contactants, including eight different constituents of her shoes, and nylons, had entirely negative reactions

B Reactions to scratch and intradermal tests with common dust-borne allergens were completely negative

C A number of sharply positive reactions to scratch tests with foods were obtained, and it was Dr Ingraham's opinion that these were of a type which would



Fig 6 (case 4) —There was an important contributory pyogenic factor in this patient's eruption, and evaluation of the food allergy factor was not possible until the bacterial infection was treated concomitantly

make one feel that they could be of significance The foods producing positive reactions were almonds, apples, asparagus, bananas, beets, broccoli, carrots, cashew nuts, cauliflower, American cheese, Roquefort cheese, cherries, cinnamon, coconut, coffee, dates, dill, eggplant, lemons, mushrooms, oats, oranges, peanuts, white potatoes, prunes, spinach, turkey, watercress and wheat During this two week period there was no restriction of the patient's diet and no improvment

2 Within one week after she was placed on a scratch test–negative diet, there was 75 per cent improvement in all lesions, with decrease of pruritus Two weeks

When the patient consulted us, she had seven distinct, rather well demarcated, erythematous, oozing, scaling, vesicular plaques on the dorsal surface and sides of three fingers of the right hand, two fingers of the left hand and the right palm There was some crusting but no frank vesicopustules In addition, she had superficial fissures in several plaques, and there was some limitation of movment of the involved fingers The only other finding of importance was an erythematous, edematous, scaling, well demarcated plaque on the inner surface of the right upper eyelid The latter lesion had been noted about two weeks previously



Fig 2 (case 22) —The exacerbation which is illustrated followed the ingestion of smoked pork Concomitant bacterial infection was a complicating factor

The familial and personal allergic history were noncontributory except that the patient had had what had been diagnosed as allergic vasorhinitis on one occasion when she was living in Texas There was no history of any type of previous cutaneous disease or intolerance to any contactants encountered during her work as a nurse prior to the onset of her present trouble

The management and course of this patient's eczematous dermatitis during the seven months' observation period were as follows

1 She was advised to discontinue work, which she did for a three week period, and during this time Dr Norman Ingraham Jr did a complete allergy work-up,

SUMMARY STUDY AND TREATMENT OF PATIENTS

The successful study and treatment of these 26 patients from the food allergy point of view was accomplished by the following methods (1) strict trial diet including hospitalization, for 11 patients, (2) basic "nonallergic" diet, for 9 patients, (3) "spot" elimination diet, for 5 patients, and (4) scratch test–negative diet, for 1 patient

Furthermore, attention to other factors, including careful study and elimination of contactants and primary irritants, elimination of the use of drugs (internal) in several patients, and treatment of the pyogenic factor, was necessary in 12 of the 26 patients Cure was obtained in only 54 per cent of these 26 patients by determination and elimination of the responsible food allergens alone

At the same time, it is emphasized that food allergy was such an important contributory factor in the disorders of the other 46 per cent of the patients in whom it was not the only etiologic factor that a satisfactory therapeutic result could not have been accomplished without the discovery and elimination of the allergic foods

From these data, it would seem that any single dietary method of approach, without consideration of other factors, will result in misconception with regard to the possible primary or contributory food sensitivity factor, and resultant therapeutic failure In those patients in whom a food sensitivity is the only etiologic factor, prompt improvement and a clinical cure will follow the institution of a suitable elimination diet We agree with Flood and Perry that the strict trial diet will result in the highest percentage of cures, but the basic nonallergenic diet which we have used on an outpatient basis will be effective for a significant number of patients for whom food allergy is the only etiologic factor The so-called "spot elimination diet," which simply provides for the interdiction of a small number of foods of high allergenic index, will effect a cure in a fairly small percentage of patients The failure of any particular dietary regimen tends to discourage the patient and makes it difficult for one to institute a more rigid dietary approach In general, it is preferable for one to outline a diet which informs the patient what he is to eat, rather than one which tells him what he is not to eat In the other large group of patients, in whom food sensitivity is only a contributory concomitant factor of varying importance, study and treatment is much less rewarding therapeutically, without hospitalization, it is most difficult for one to untangle and treat the multiple etiologic factors involved

INCIDENCE OF FOOD ALLERGY IN ETIOLOGY OF ECZEMATOUS DERMATITIS

It is difficult for one to evaluate accurately the role of food allergy in the etiology of eczematous dermatitis so far as the exact incidence is concerned In the first place, it is not possible for one to exclude food

of foods to be eliminated at this time because it is most difficult for one to avoid these foods in a hospital dining room

4 The patient had some improvement in her condition in the next two weeks, but continued to have periodic flare-ups, although they were less severe than previously At this time wheat was added to the foods to be eliminated from the diet

5 There was no change in the next week, and at this time it was decided to add eggs to the interdicted foods, which action meant that the total restriction of the diet included the elimination of almonds, bananas, lima beans, Roquefort cheese, cherries, cinnamon, chicory, coconut, dates, grapefruit, milk, mustard, onion and poppy seed, which had been eliminated on the basis of positive reactions to scratch testing, and chocolate, coffee, orange, cheese, tomatoes, nuts, wheat and eggs, which had been eliminated in an effort to obtain a so-called basic nonallergenic diet

6 During the next two weeks, after the elimination of eggs from the diet, there was more sustained improvement than at any previous time since the patient had come under our observation, and for the first time there was complete absence of pruritus and no appearance of new vesicles within the last week

7 Five days later the patient had a distinct flare-up at all previously involved sites, including the eyelid, characterized by pruritus, vesiculation, oozing, erythema and edema This exacerbation occurred approximately six hours after she had eaten one boiled egg It subsided entirely within five days

8 After this development, the patient remained free of symptoms and lesions except for four exacerbations, all of which subsided promptly The first such exacerbation did not occur until she had eaten one egg daily for three days, the second, until she had eaten one egg daily for six days, and the third, until after she had increased her intake of milk to one quart daily for three consecutive days During the next six weeks all other interdicted foods were added, without any exacerbation, so that, at the end of this time, the restriction of her diet included only the elimination of eggs and the limitation of milk to one glass daily, with no restriction of foods containing milk

9 During the next three months her hands and eyelid remained clear, despite the addition of all foods containing eggs to her diet, although she continued to restrict eggs to three weekly (one every other morning for breakfast) She had continued to work as a nurse and had done all her own housework, with avoidance of furniture polish, procaine hydrochloride, penicillin and streptomycin, but with no other restrictions or precautions

The diagnosis was eczematous dermatitis of the hand and left eyelid, due to allergic contactants (penicillin, streptomycin, procaine hydrochloride and o'cedar® furniture polish) and food allergy (eggs and milk)

Comment It seems apparent that this patient originally had an allergic contact eczematous dermatitis and that the food allergy factor did not enter the picture until approximately six months after the onset of her dermatitis, which gradually increased in severity, presumably because of repeated exposure to the allergic contactants It is obvious that the responsible foods would have been discovered promptly if this patient had been hospitalized or if a resrticted elimination diet had been put into effect early in our observation period When egg was added to the diet one week after pronounced improvement had occurred, a

characteristic in that they are fairly well demarcated, erythematous, edematous and slightly scaling and in many respects resemble a fixed drug eruption

Individual lesions vary considerably In the vast majority of patients there is a vesicular element, although vesiculation may be absent There is a tendency to oozing and superficial fissuring, and in many persons vesicopustules and other signs of secondary pyogenic infections are dominant when the patient is first seen In general, the borders of plaques are not well demarcated, and they are not annular with a tendency to central clearing Pruritus, which is usually intense, is a regular feature of eczematous dermatitis due to food allergy The itching is periodic and varies from day to day unless one of the causative foods is eaten daily

When food diaries are used as a method of study, pruritus is almost as dependable as a sign of an exacerbation as is the appearance of new vesicles and other objective evidence

However, unfortunately, there are no absolute diagnostic criteria in distinguishing eczematous dermatitis due to food allergy from that due to other factors, but with experience it is possible for one to acquire a "high index of suspicion"

COURSE OF ECZEMATOUS DERMATITIS DUE TO FOOD ALLERGY

In most cases there is a history of a tendency to spontaneous exacerbations and partial remissions We have not been particularly impressed with a change of incidence in relation to the season of the year, although in general the process tends to be severer during the winter months

Quite uniformly, rapid, significant improvement has been noted in one to three days when the causative foods were eliminated, provided that the etiologic picture was not complicated by other factors, such as contactants and pyogenic infection Exacerbations which follow addition of an allergenic food have occurred within fifteen minutes after a small serving of a particular food, and, almost always, objective evidence of such exacerbations is preceded by pruritus On the other hand, the interval between ingestion and exacerbation has been as long as forty-eight hours after the food was eaten, and in 3 of our patients exacerbations did not occur until the food had been eaten on six consecutive days It seems quite certain that exacerbations occur more promptly and with a smaller quantity of the allergenic food if the addition to the diet is made within a few days after the initial lesions have become quiescent Many patients have been observed in whom decided prompt exacerbations occurred after ingestion of a given food soon after initial improvement had occurred on a trial diet, several weeks or months later, these same patients failed to have such exacerbations following the addition of the same food to the diet It would

This condition had had its onset as a rather small, coin-shaped, pruritic, scaling, eczematous plaque on the inner surface of the right foot, approximately fifteen months before the patient consulted us Soon afterward, there had been progressive extension and increase of pruritus, which was intense and occurred in paroxysms The course had been characterized by repeated exacerbation and partial remission, but complete clearing had not occurred at any time, and pruritus had not been absent for more than one or two days at a time The patient had been under the care of a radiologist, who had given her approximately fifteen roentgen ray treatments, during which course of therapy she had had partial improvement and one lesion which had appeared on the flexor surface of the wrist had disappeared



Fig 5 (case 24) —In some respects case 24 was one of the most interesting in our series despite the apparent insignificance of the involvement The lesion resembled a fixed drug eruption It had persisted for almost three years and disappeared within seven days after the responsible food allergens were eliminated Numerous prompt exacerbations were demonstrated on the addition of food allergens to the diet

entirely She had received a total of 1,500 r to all affected sites Soon after the roentgen ray treatments were discontinued, there had been progressive increase of involvement, and for this reason the radiologist had referred her to us The management and the course of her eczematous dermatitis during the twelve month period of observation were as follows

1 Hospitalization was strongly advised, but this was not possible All previous local medication, which had been quite varied, was discontinued, and 3 per cent

string beans, lima beans, chicken, sweet corn, vanilla extract, rye, sweet potatoes, cheese, paprika and white potatoes At the present time another patient, for whom the primary food allergen is beef, is under observation, as is another, for whom canned pears are the most important food allergen

COMMENT

It should be emphasized particularly that, while allergic sensitivity to foods is an important reason for chronicity and persistence of an eczematous eruption, it is not an etiologic factor for even a majority of such patients, and study and treatment of the patient in this regard must be carried out with scrupulous regard for the many other possible etiologic factors concerned In addition, as with many other methods of treatment, too great enthusiasm or "faddism" for diets may have a medically deleterious effect on the whole patient Prolonged restriction of caloric intake, particularly for underweight patients, for many growing children or for the aged is obviously unjustified Likewise, the balance of various fractions in the diet and the adequacy of vitamin intake must receive thoughtful consideration Some patients will cooperate too enthusiastically for their general medical good and may continue to follow severely restricted diets for too long a time and with too little justification

In general, local treatment was not particularly helpful in the management of this series of cases, except in those in which bacterial infection was an important contributory factor Also, superficial roentgen ray therapy does not seem to influence significantly the course of eczematous dermatitis due to food allergy More than 50 per cent of our 26 patients had had an adequate trial of roentgen ray treatment, and, although apparent partial initial improvement had been noted in some patients, the end result was unsatisfactory in all cases in that relapse occurred within a short time after the treatment was discontinued Penicillin administered parenterally was useful in controlling pyogenic infection when this was a complicating factor

The history in regard to food sensitivities and other allergic manifestations prior to the onset of the presenting dermatitis was not particularly helpful in the initial evaluation of these patients There was a family history of allergy for 15 per cent of the patients and a personal allergic (not atopic dermatitis) history for 15 per cent, although the two groups were not identical

The psychogenic factor seemed to be important for several of our patients, and indeed our experience with the present series leads us to believe that there is an emotional component in the background of the vast majority of persons with food sensitivities For this reason, one must be careful to evaluate each patient critically and include in the

later, there was no additional improvement Therefore, she was asked to try for one week a basic "nonallergenic" diet consisting only of apricots, peaches, canned pears, prunes, sugar, tea, beans, chicken, string beans, lamb, lettuce, cabbage, peas, ry-crisp,® corn bread, salt, sweet potatoes, turnips, peach preserves and apricot preserves After one week on this diet, she had complete relief of pruritus and all signs of involvement, except for residual hyperpigmentation, scaling and very slight lichenification, had disappeared

3 At this time, she went on vacation and disregarded her diet entirely On successive days, she ate sea food dinners and chocolate candy—indeed, there was no interdiction of foods Within twelve hours after the first such meal, there was pronounced recurrence of pruritus, followed by a sharp, severe exacerbation involving all previously affected sites During the next three weeks, she resumed her scratch test–negative diet except that chocolate, nuts and all sea foods were added to the interdicted foods The pruritus disappeared within three days, and regression of objective signs gradually occurred except for one exacerbation possibly associated with the ingestion of watermelon At the end of three weeks, the patient was free from pruritus, and only residual hyperpigmentation and slight scaling persisted at the previously involved sites

4 During the past eight months, this patient noted repeated exacerbations following the attempted addition of the following foods to her diet wheat bread, or wheat flour in any form, chocolate, shrimp, crab meat, lobster and coffee In the last three months, she has been able to drink an occasional cup of coffee without exacerbation except for transient pruritus She has found that complete elimination of wheat products for a period of two or three weeks, as well as interdiction of chocolate, shrimp, crab, lobster and coffee, is followed by complete absence of all signs of involvement Furthermore, if the ingestion of wheat products is limited to two pieces of part rye and part wheat bread daily, pruritus and scaling of previously affected sites are so minimal that they do not interfere with any of her activities, therefore, she prefers to accept these consequences rather than eliminate bread entirely Repeated attempts to increase the amount of wheat-containing foods resulted in decided increase of pruritus of the eczematous patches at approximately the original sites of involvement

The diagnosis was eczematous dermatitis, due to food allergy (wheat, chocolate, coffee, shrimp, crab and lobster), of the hands and feet

Comment The initial elimination diet, which was based on scratch test–negative foods, happened to exclude the principal food allergen, which was wheat, and, also, it resulted in the interdiction of coffee, which was a relatively unimportant food allergen Complete improvement did not occur on this dietary regimen because of other specific food sensitivities in the form of several different sea foods and chocolate, all of which produced negative reactions in scratch tests Complete relief of symptoms and disappearance of pruritus followed a brief period of pronounced dietary restriction, which happened to exclude all the responsible food allergens It is probable that this patient could have been cured by a brief period of hospitalization and the use of a strict trial diet The rapid response to interdiction of foods would have made it possible to add foods rather rapidly, and within one month she could have been placed on a quite adequate diet

6 Scratch tests with foods were of almost no value in the management of these patients

7 The methods of approach in the study of these patients are discussed in some detail Ideally, the vast majority should be hospitalized for an adequate evaluation from the standpoint of food allergy, for about 40 per cent of our patients such evaluation would not have been possible without hospitalization However, with a fair percentage of cooperative patients, satisfactory elimination diets can be put into effect on an outpatient basis, especially if food allergy is the only etiologic factor involved

8 The necessity of evaluating and treating such patients along broad etiologic lines as well as with respect to food allergy is emphasized and illustrated in the case histories of many of our patients

9 Chocolate, oranges, wheat, pork, eggs, sea food, tomatoes, grapefruit, nuts and milk were encountered more frequently as food allergens in this series of patients, but specific food sensitivity was demonstrated to twenty-six other foods by one or more patients Sensitivity to two or more foods was demonstrated by 24 of the 26 patients

10 It is believed that food allergy is one of the important etiologic factors in eczematous dermatitis In our experience, food allergy is the only etiologic factor or a significant contributory factor in the case of 16 to 18 per cent of patients with chronic eczematous dermatitis of the hands and/or feet

11 The technic of management and interpretation of results are relatively difficult, especially in the cases of those patients for whom food allergy is only one of numerous possible etiologic factors

Department of Dermatology, University of Texas School of Medicine

133 South Thirty-Sixth Street

ABSTRACT OF DISCUSSION

DR SAMUEL M PECK, New York I wish to congratulate Dr Livingood for the fine piece of work which he did and especially for his patience in carrying out this type of rather ungrateful research The average dermatologist is somewhat prone to disregard the value of the approach which Dr Livingood has made because, on the one hand, it is so time consuming and, on the other, the results in many instances are most disappointing I think the chief difficulty in this problem is the fact that one is unable to judge on clinical evidence alone which cases are due to foods and which are due to the many other factors which can give the same clinical syndrome Also, it is very rare to have a factor such as food sensitivity play other than a major or a minor role in the dermatitis Food plays a role in infancy and childhood as the sole cause of eczema This point no one will deny However, it is difficult for many to visualize a dermatitis which is limited to the hands as being mainly due to a food factor Certainly, in the eczema of infancy and childhood, one rarely, if ever, sees limited localization, especially as far as the hands are concerned It would be a great help if there

allergy as an etiologic factor in a given case unless the patient is hospitalized and placed on a strict trial diet and unless there is the elimination of other possible contributory factors, such as pyogenic infection and contactants, which might obscure a concomitant food sensitivity Obviously, such a procedure is not feasible in a fair percentage of cases Furthermore, the experience of various investigators will differ considerably For example, physicians in industry will encounter a higher incidence of eczematous dermatitis due to allergic contactant and primary irritant factors It has been our experience that food allergy is the only significant etiologic factor for about 7 to 8 per cent of the patients with chronic eczematous dermatitis and an important contributory factor for an additional 8 to 10 per cent of such patients The common concomitant factors which were recognized in the present series of 26 patients include allergic contactant, primary irritant, pyogenic infection and sensitization and drug allergy

DESCRIPTION OF LESIONS

We agree with Sulzberger that if food allergens cause eczematous eruptions of the hands "then foods must be considered as possible etiologic agents in other eczematous eruptions no matter what their localization", and it has been our experience that such eruptions due to specific food sensitivity do occur at other sites on the cutaneous surface

We have recorded the following sites of involvement in one or more patients all surfaces of the hands and feet, the eyelids, the forearms, the upper arms, the legs, the thighs, the face, the neck, the groins, the posterior surface of the scrotum, the axillas, the external auditory canals, the trunk and the buttocks It is true that the hand is the site of predilection, but this is certainly not the only site of localization In our series of cases, the hands were involved in 21 of 26 patients, the dermatitis was limited to the hands with no other involved sites in only 10 of the 26 patients

Eczematous dermatitis due to food allergy tends to be patchy rather than diffuse The dorsal surface and sides of the fingers, the palms, the dorsal surface of the hands and the interdigital spaces occasionally have been sites of localization which we have noted on the hands On the feet, the patches tend to be localized on the inner and dorsal surfaces of the feet, although the distribution may be on the dorsal surface of the toes, suggesting an allergic contact dermatitis, or on the plantar surface of the feet, suggesting dermatophytosis Usually the involvement is in the form of plaques, although patients with diffuse involvement of the axillas and groins, as well as with diffuse involvement of the extremities, have been observed The eyelid lesions are quite

was the percentage of cases in which skin tests with food were helpful? Did any adults in the series that were found to be sensitive to food give any history of having been previously sensitive to that particular food, or had they always enjoyed that food in the past? How long did this newly discovered food sensitivity last? Was it permanent, or did it clear up after the other factors had been removed?

DR MARION SULZBERGER, New York I wish to compliment Dr Livingood and Dr Pillsbury on an excellent paper The first point I should like to emphasize is that no one who has not attempted to carry out exact diets on ambulatory patients can realize how difficult the task is My own results with this method in the last fifteen years have been on the whole very unsatisfactory I should like to point out that it is almost prohibitively difficult for the patient to carry out a rigid elimination diet While on such diets the patient can join in almost no social activities—no eating out, no lunches while away from home, no participation in meals with others and no snack or candy or drink between meals, for example I have found that under these conditions patients either make involuntary slips or keep cheating The second point I should like to stress is that it is now obvious that atopic dermatitis has an eczematous phase This is true, not only in infants but in adults, although in the latter it is not as uncommon This form of atopic eczematous eruption may, of course, be susceptible to flare-ups following exposure to allergenic foods, just as are some cases of infantile eczema And in adults atopic eczematous eruptions can and do appear on the hands, particularly the dorsa of the fingers

Did Dr Livingood exclude the external contact with foods? It is difficult for one to eat bread or oranges, for example, without letting them touch the hands I think that in order to come to the conclusions that these eruptions are due to ingestion of foods, one must always and absolutely exclude the possibility of external contact, and I feel certain Dr Livingood has done this

I enjoyed the presentation and should like to suggest that Dr Livingood and Dr Pillsbury may in the future find it advantageous to attempt to classify their cases of "hand eczemas" into two large groups, namely, those of nonatopic and atopic dermatoses

My impression is that the results following elimination of certain foods would be much greater in atopic persons than in the nonatopic ones Moreover, for reasons which I mentioned in discussing aberrations of sweating, the role of foods and drugs in exacerbations of dyshidrosis may merit careful scrutiny in the future

DR CLARENCE S LIVINGOOD, Philadelphia I wish to thank the discussers Many of the questions brought up in these discussions are answered in our paper In answer to the questions of Drs Sulzberger and Osborn, with reference to external contact with food, rather than ingestion, as a factor We had thought of that point, and it has been our experience that eczematous lesions in some cases are caused by contactant sensitivity to foods, especially citrus fruits and vegetables However, in our series of cases, external sensitization to foods was a minor factor in comparison with endogenous allergy to foods We have been careful in evaluating this particular question, and, for example, in some cases suspected foods were given in capsule form

The duration of sensitivity to a particular food or foods varies in individual cases In some of our cases the sensitivity disappeared within several weeks after the lesions had disappeared, in others repeated exacerbations could be reproduced as long as six to eight months after the involution of the eruption, and in some it is probable that the sensitivity persists indefinitely We agree with Dr Peck that the allergic pattern in regard to food sensitivity in a given case is likely to change over a period of years

seem that in many instances spontaneous desensitization takes place, and several months after disappearance of the patient's dermatitis foods which caused definite exacerbations previously may be taken without resultant symptoms or signs in the skin

Our experience is at variance with that of Rowe [7b] in that we believe that significant improvement is evident within several days to one week, provided that all the allergenic foods are eliminated from the diet and provided that all other contributory factors have been eliminated and treated Those patients who have other etiologic factors in addition to food allergy will not improve significantly on a therapeutic approach which is designed to find and eliminate only the food allergy factor

It is our opinion that the process in many of these patients had its onset as allergic contact dermatitis, and in others as a primary pyogenic dermatitis, for example Later on in the course of the disease, the specific food sensitivity factor became operative and in many instances became the chief perpetuating factor in the eruption Also, the reverse was true in that in some instances the eruption had its onset as an eczematous dermatitis due to foods and subsequently other factors, such as allergic contactants, invasion and sensitization by bacteria, complicated the process As in allergic contactant dermatitis it is advantageous for one to treat eczematous dermatitis due to food allergy early in the course of the disease because it is easier to effect a cure under these circumstances This point was well illustrated in many of our cases

INCIDENCE OF SENSITIVITY TO VARIOUS FOODS

This series of patients is too small for analysis as to the relative frequency with which individual foods may sensitize the skin, but it is interesting to tabulate the results for what they are worth In 1 or more patients the allergenic role of the following foods was demonstrated in our series of 26 patients, and in almost all instances exacerbations were noted on 2 or more occasions

Food	No of Patients	Food	No of Patients
Chocolate	9	Grapefruit	5
Sea food *	8	Tomatoes	4
Wheat	6	Eggs	4
Oranges	6	Broccoli	2
Pork	5	Rice	2
Milk	5	Cinnamon	2
Nuts	5	Smoked pork	2

* Lobster, 2, crab, 2, shrimp, 2, clams, 1, and shad, 1

Specific sensitivity to the following foods was encountered in 1 patient peaches, carrots, onions, peas, Scotch whisky, butter, veal, pepper, cauliflower, pimento, coffee, pineapple, tea, apricots, cabbage,

entity and to advise regarding corrective measures After atrophy of the follicles has taken place no method of treatment would be likely to succeed If the causative factors are eliminated early enough, complete recovery takes place, according to the aforementioned observers

REPORT OF CASES

CASE 1—D H, a girl aged 18, came in primarily for the treatment of acne of a moderate degree of activity In addition to the acne examination revealed a pronounced thinning of the hair along the sides of the scalp above the ears, where the hair was pulled up toward the top of the head in tight braids Scattered through the areas of partial alopecia were a number of small follicular papulopustules

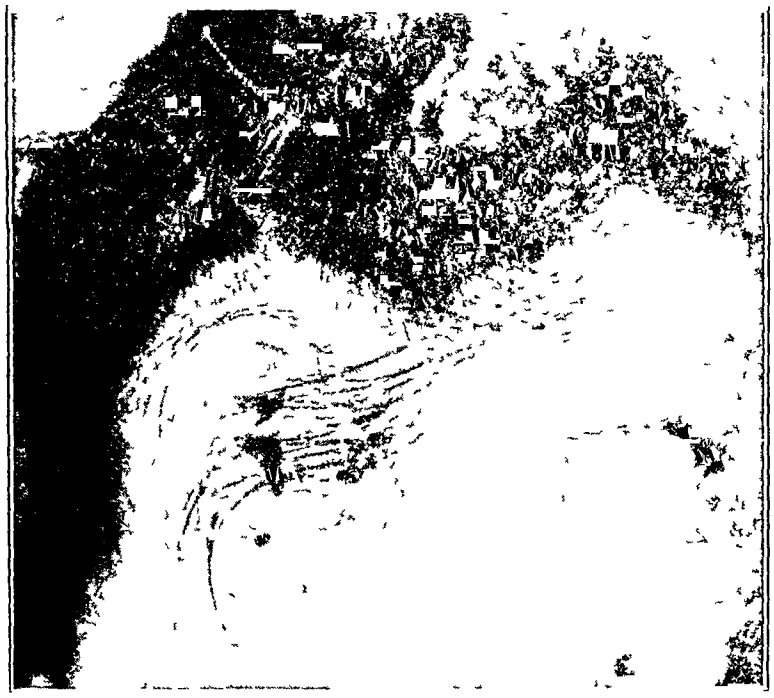


FIG 1 (case 1)—Area of alopecia in front of and above ear, due to constant traction from tight braids

CASE 2—A C, a girl aged 18, came to the office primarily for the treatment of redness, crusting and slight swelling of the eyelid margins, characteristic of blepharitis Examination revealed, in addition to the condition of the eyelids, a moderate degree of thinning of the hair on both temple areas in front of the ears There were a number of broken hairs, some of them with an exclamation point appearance, and a few follicular pustules scattered through these areas The patient had been in the habit of using metal curlers on the sides of her scalp for the preceding four months She thought that the thinning of the hair was of about six weeks' duration

CASE 3—E W, a woman aged 65, presented herself with a complaint of an eruption on the sides of the scalp, associated with a thinning of the hair which had been present for about six months The patient had been using metal curlers at night

group of persons with food allergy only those patients who have definite repeated exacerbations following the addition of causative foods to the basic diet It is conceivable that at least some of these patients could be cured with ideal psychiatric treatment, but this approach has had limited usefulness in our experience This principle was illustrated in the case of 1 patient who had repeated exacerbations of her dermatitis after the ingestion of small quantities of grapefruit during a period of considerable emotional strain incident to working under an exacting employer, some months later, under more favorable circumstances of employment, it was possible for her to eat several times as much grapefruit with only minimal pruritus and very few objective signs of involvement

It is essential for one to realize that there is an appreciable individual variation in the course of patients who have eczematous dermatitis entirely or in part due to specific food sensitivity In some cases a prompt regression of the dermatitis is noted after the interdiction of the responsible foods, in others significant improvement does not occur for as long as seven to ten days The same variation applies to the onset of an exacerbation following the addition of a causative food, although in the vast majority of cases such exacerbations are seen within a period of forty-eight hours It is not a simple procedure to manage the patients successfully, and considerable experience is necessary before one acquires an appreciation of the problems involved The physician who follows a stereotyped approach will not cure a significant percentage of patients with cutaneous food allergy

SUMMARY AND CONCLUSIONS

1 A series of 26 patients with eczematous dermatitis, for whom it was demonstrated that specific sensitivity to various foods was the only etiologic factor or a significant contributory factor, is presented

2 The chief localization site encountered was the hands (involved in 81 per cent), although the feet, eyelids, legs, arms, face, scrotum, groins, neck, buttocks, perianal region and axillas were also involved in 1 or more of our patients

3 In addition to food allergy, other concomitant etiologic factors, including allergic contactants, primary irritants, pyogenic infection and pyogenic sensitization and allergic drug factors, were demonstrated for 12, or 46 per cent, of these 26 patients

4 Eczematous dermatitis due to food allergy tends to occur in localized, rather inflammatory plaques, oozing, vesiculation and excoriations were noted in a high percentage of cases Apparent spontaneous exacerbations and partial remissions are relatively common

5 Pruritis, which was usually quite severe, was a regular and prominent feature of the process

SUMMARY

Five cases are reported of traumatic marginal alopecia in white women

The clinical appearance consists of a triangular area of partial alopecia involving the sides of the scalp above or in front of the ears, usually accompanied by folliculitis and atrophy of the follicles

The condition is believed to be caused by persistent traction on the hair from vigorous and prolonged brushing, a tight hairdress or the use of curlers Previously reported cases of this condition have occurred in Negroes or mulattoes

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were a simple approach to establish or rule out foods as etiologic factors I have attempted to find one in many instances, but so far, the necessary procedure still boils down to the tedious, long-drawn-out, trial and error type of approach One thing should be emphasized, namely, that, as I believe, in different parts of the country and probably among different classes of population different combinations of factors are responsible for the dermatitis on the hands In the few cases in which I believe I have definitely established food allergy as a cause of eruptions on the hands, nearly all the patients were females If this observation is common, I think it should be helpful Furthermore, when a patient with a dermatitis on the hands presents himself or herself to me, I automatically lean away from consideration of food as an etiologic factor in the dermatitis of the hands in men, for them fungi, bacteria and contact factors are the predominating etiologic agents In women, bacteria or molds will also play a role if the eruption is present long enough I should like to cite 1 case which to me was enough payment in satisfaction and compensated for all the failures with this approach This was of a young married woman who came to me with a dermatitis of the hands of months' duration I automatically went through the routine procedures of looking for an infectious agent and for household contacts as the cause of her dermatitis I totally disregarded the fact that I had treated her successfully for food allergies as the cause of her infantile eczema In looking over her old records, I found mention of this, and when she eliminated the foods to which she had again become sensitive over the years, the dermatitis on her hands finally cleared up One must bear in mind that, even when the offending foods are removed, there is no dramatic improvement Patience and a thorough understanding of all the factors which contribute to the dermatitis are all needed in order for one to treat one of these patients successfully I wish to congratulate Dr Livingood and Dr Pillsbury for an excellent paper

Dr Earl D Osborne, Buffalo I, too, wish to congratulate Dr Livingood and Dr Pillsbury on having cured anyone with a condition having a food factor in an allergic background It is a very difficult job to undertake There are a few observations I should like to make First, I do not believe that it has been proved that protein substances as such will produce eczematous reactions When one speaks of foods, one must realize that one is talking about a very chemically complex subject Foods contain not only proteins but also fats, carbohydrates and a multiplicity of oleoresins I should like to ask Dr Livingood whether he did any patch testing in his cases with oleoresins present in the various foods It appears to me that it is possible for one to explain many apparent recurring vesicular eruptions of the hands on the basis of the ingestion of specific oleoresins present in various foods It is known that in the case of poison ivy and other weed dermatoses a flare-up of a preexisting eruption on any part of the body can be produced by the ingestion of the specific or related oleoresin concerned I believe that specific hypersensitivity does exist to the oleoresins in many fruits and vegetables, both from local contact and, in recurrences following this, from the ingestion of the specific oleoresin Finally, it is my belief that investigation will show that when foods are at fault in the production of an eczematous eruption the responsibility is probably that of the oleoresin content and not of the protein, carbohydrate or fat content of the particular food

Dr Eugene F Traub, New York I, too, enjoyed Dr Livingood's presentation and wish to thank him I should like to ask him several questions Were the cases in which the condition appeared to be influenced by or to react to certain foods discovered through the use of test diets, or did the patients react positively to tests with food to which they were not otherwise known to be sensitive? What

made, while in tinea cruris, unfortunately, no dependable correlation could be found The results of study will be discussed for each category, in the following order tinea pedis, tinea unguium, tinea cruris, tinea manus and generalized tinea

TINEA PEDIS

Of the 360 positive cases of tinea pedis, a fungus was isolated in 186, or 51 per cent T gypseum was cultured in 118 cases (63 per cent), Trichophyton rubrum in 58 cases (31 per cent), Epidermophyton floccosum in 4 cases (2 per cent) and C albicans in 6 cases (3 per cent) In other words, T gypseum was encountered about twice as frequently as was T rubrum, and both E floccosum and C albicans were rarely found If only the three dermatophytes are considered, T gypseum was isolated in 64 per cent of the cases, T rubrum in 34 per cent and E floccosum in 2 per cent

The latter figures agree favorably with those of the results obtained by Miss Rhoda Benham, as detailed by Hopkins and associates,[5] who credited her with 111 positive cultures for the periods of 1940 and 1946 The incidence of T gypseum obtained by Benham averaged 64 per cent, that of T rubrum, 25 per cent, and that of E floccosum, 5 per cent Percentages obtained by Lewis and Hopper[6] in 1938 for 153 cultures were not dissimilar T gypseum, 73 per cent, T rubrum, 25 per cent, and E floccosum, 2 per cent

Six types of lesions were identified in cases of tinea pedis chronic intertriginous, chronic hyperkeratotic scaling, chronic papulovesiculosquamous, bullous, subacute and severe chronic hyperkeratotic scaling Table 1 details the total number of cases of each of these types, the percentage in which cultures were obtained and the percentage of each of the etiologic agents

Chronic intertriginous lesions accounted for 41 7 per cent of the 360 clinical cases noted Cultures were obtained from 48 per cent of the cases In this type of lesion it is almost impossible to determine the etiologic agent by clinical examination alone T gypseum was isolated in 54 3 per cent, T rubrum, in 36 per cent, and E floccosum and C albicans, in 1 4 per cent and 8 3 per cent, respectively

Chronic hyperkeratotic scaling lesions of the plantar and medial surfaces ranked second, comprising 19 per cent of the 360 cases Cultures were obtained in only 37 1 per cent of the cases, the majority

4 Footnote deleted on proof

5 Hopkins, J C , Hillegas, A B , Ledin, B L , Rebell, G C, and Camp, E Dermatophytosis at an Army Post, J Invest Dermat 8 291 (June) 1947

6 Lewis, G W, and Hopper, M E An Introduction to Medical Mycology. Chicago, Year Book Publishers, Inc, 1939

TRAUMATIC MARGINAL ALOPECIA IN WHITE WOMEN

SAMUEL AYRES Jr, M D
SAMUEL AYRES III, M D
AND
JOSEPH I MIROVICH, M D
LOS ANGELES

COSTA and Junqueira[1] recently summarized the literature on traumatic marginal alopecia, which, according to their observations and those of Ribeiro,[2] occurs almost exclusively in Negro and mulatto women They pointed out the similarity between this condition and alopecia liminaris frontalis as described by Sabouraud[3] and expressed the opinion that both conditions are caused by stretching the hair in tight braids or "buns" and, especially in the case of Negro women, by efforts to straighten kinky hair Folliculitis frequently results from this constant traction, and, with or without folliculitis, atrophic changes of the follicles gradually develop and lead to permanent alopecia

In the cases described by Ribeiro and by Costa and Junqueira the alopecia occurred in triangular areas involving the temples, with the apex pointing downward in front of the ears

Inasmuch as the previously reported cases of this entity occurred exclusively in Negro or mulatto women, except for 1 case in a white woman, mentioned by Ribeiro, it seemed worth while to record 5 cases in white women

In view of the fact that the alopecia tends to be permanent if the trauma due to traction from tight hairdress or excessive brushing is allowed to continue, it becomes important for one to recognize the

1 Costa, O G, and Junqueira, M de A Traumatic Marginal Alopecia Due to Traction on the Hair A Comparative Study of Alopecia Liminaris Frontalis of Sabouraud, Arch Dermat & Syph **48** 527-532 (Nov) 1943

2 Ribeiro, H Alopecia marginal traumatica por tracção dos cabellos, Brasil-med **52** 1267-1271, 1937, Alopecie marginale traumatique, Ann de dermat et syph **9** 495-503, 1938

3 Sabouraud, R, in Darier, J, and others Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, pt 7, p 13, De l'alopecie liminaire frontale, Ann de dermat et syph **2** 446-460, 1931, Diagnostic et traitement des affections du cuir chevelu, Paris, Masson & Cie, 1932, p 398, Pelades et alopecies centraires, ibid, 1929, p 93

and E floccosum in the second Of the chronic papulovesiculosquamous lesions, T gypseum was the etiologic agent in three fourths and T rubrum in the others Four fifths of the subacute lesions may be assumed to be caused by T gypseum It is not possible to identify by clinical examination alone the fungous species in chronic intertriginous lesions

In addition to the foregoing conclusions, one may infer from the material in table 1 that T rubrum is more difficult to isolate than is T gypseum In the five types of tinea pedis due to species of Trichophyton, the greater the percentage of lesions from which the organism was isolated, the higher the incidence of T gypseum noted For instance, cultures from bullous lesions yielded the etiologic agent in 74 per cent of lesions, T gypseum being isolated in each case, while cultures from chronic hyperkeratotic scaling lesions yielded the agents in only 37 1 per cent of all lesions, T gypseum being noted in 15 4 per cent and T rubrum in 84 6 per cent One may infer that the incidence of T rubrum would be much higher in the case of chronic hyperkeratotic, chronic papulovesiculosquamous and chronic intertriginous scaling, and even subacute lesions, if cultures were obtained from all cases listed

TINEA UNGUIUM

Among the 429 cases of dermatophytosis, there were 245 cases of tinea unguium, of which 222 cases were of infected toe nails and 23 of infected finger nails Infection of the toe nails was noted and proved by laboratory examination in 60 per cent of the cases of tinea pedis Hopkins and associates [5] had observed infected toe nails in 47 per cent of their cases of recurrent tinea pedis

At first, the number of nails involved and the degree of involvement were believed to be of primary importance, but it soon became apparent that there was some correlation between the organism isolated and certain types of involvement of the nail Therefore considerable effort was expended in an attempt to obtain a reliable key which could be used by physicians interested in this problem It is not felt that this key is a complete answer, but it is believed that it forms a basis for future and more exhaustive study

As in cases of tinea pedis, six types of lesions have been noted in cases of tinea unguium, the last two types have been observed only on the hands

Type 1 Leukonychia trichophytica, consisting of white patches on the surface or within the nail plate T gypseum has been reported as the agent always isolated, however, the mycology laboratory isolated T rubrum in 3 out of 5 cases in which cultures were obtained

Examination revealed a diffuse thinning of the hair over the scalp, with a mild seborrheal scaling Involving each temple area in front of the ears there was a more pronounced loss of hair, with a few broken hairs and empty follicles Just above this area on both sides was a transverse erythematous and slightly elevated ridge or streak which the patient stated coincided with the area covered by the metal curlers There were a few follicular papules in this erythematous area A patch test with the patient's aluminum curler gave no reaction

CASE 4—D H, a girl aged 11, had noticed thinning of the hair, with irritation along the temples, for about two weeks The patient had been in the habit of rolling her hair tightly with metal curlers at night and had been spending a great deal of time every day brushing her hair upward along the sides

Examination revealed a moderate degree of thinning of the hair along the temples in front of and just above the ears There were a number of broken



Fig 2 (case 3) —Triangular area of alopecia involving the temporal region in front of the ear due to constant traction from the use of tight curlers

hairs, one of which was shaped like an exclamation point There was also a moderate degree of redness on each side of the scalp and a number of small superficial papules, several of which were crusted A patch test was made with nickel, but the patient did not return for observation

CASE 5—E J S, a woman aged 30, had had a scalp disorder for one and a half years The patient had been in the habit of combing and brushing the hair upward from the sides and fastening it in a tight braid

Examination revealed an appreciable thinning of the hair, with some erythema, over the temporal regions Some of the empty follicles showed dark plugs, and there was evidence of atrophy throughout the areas

but also concurrent chronic hyperkeratotic scaling of the plantar surfaces The strains of T rubrum isolated in these cases are being studied because of certain morphologic variations

TINEA CRURIS

Tinea cruris ranked third in prevalence, comprising 86 of the 429 cases of dermatophytosis and cutaneous moniliasis In only 18 of the 86 verified cases was the infection limited to a single site In some of these 18 cases there was a history of possible tinea pedis In 22 cases there were two lesion areas, 18 of which were of the feet and groin In the remaining 46 cases there were three or more lesion sites

Three types of lesions were noted. "eczema marginatum" type, a solid plaque type and the erythematous, exudative monilial type Correlation of the clinical aspects with the etiologic agent has not been possible in the case of tinea cruris Cultures were obtained in only 33 7 per cent (29 cases) of the verified cases Of this number, cultures yielded T gypseum in 8 (27 5 per cent), T rubrum in 16 (55 4 per cent), E floccosum in 1 (3 3 per cent) and C albicans in 4 (13 8 per cent) This small number does not provide sufficiently valid percentages, but comparison of the figures for T gypseum and T rubrum (omitting those for C albicans) indicates that, where the true dermatophytes are concerned, T rubrum is the etiologic agent in about 66 per cent of the cases of tinea cruris

TINEA MANUS

Tinea manus ranked fourth in incidence of the clinical types of dermatophytosis In all, 254 cases of service-diagnosed "ringworm of the hands" were studied Only 48 cases were established definitely as of tinea manus The majority of the cases in which this disease was not established were characterized by vesicular and exudative lesions, located particularly on the fingers

In only 10 of the positive cases were the hands alone involved, in 9 cases the feet and hands were involved, and the remaining 27 yielded three or more positive lesion sites There was a definite racial distinction observed in that only 5 Negroes (a ratio of 1 Negro to 3 white patients) were shown to have tinea manus T gypseum was recovered from lesions on the hands of 2 Negroes and T rubrum from another

With regard to origin of infection of the hand and wrist, an interesting factor was noted One third of the patients with verified lesions had a history of having worked with motor fuels and machinery at the time of onset

SUPERFICIAL MYCOSES OF VETERANS

II Dermatophytosis and Cutaneous Moniliasis, Correlation of Clinical Manifestations and Etiologic Agent

R C BURKE, Ph D
CAMBRIDGE, MASS
AND
F E BUMGARNER, M D
LOS ANGELES

IN THE past few years several efforts have been made to correlate the fungus species with the clinical manifestations of the superficial mycoses Among these studies have been the work of Lewis, Montgomery and Hopper [1] on the clinical manifestations of Trichophyton purpureum and that of Montgomery and Caspar [2] on the clinical manifestations of Tricophyton purpureum, T gypseum and Candida albicans

In a previous paper,[3] we reported on a study of 1,000 veterans with in-service diagnoses of superficial mycoses, 466 of whom had fungous infections as proved by laboratory examination Of these, 416, or 87 1 per cent, showed dermatophytosis, and 13 (3 per cent), moniliasis The 416 patients with dermatophytosis and 13 with cutaneous moniliasis had 819 clinical manifestations of various types of dermatophytosis, falling into the commonly recognized categories of tinea pedis, tinea unguium, tinea cruris, tinea manus and generalized tinea, in that order of incidence

Slides and cultures were made in each case in an attempt to correlate the various types of lesions with the etiologic agents In general this correlation was most successful with tinea pedis and with tinea unguium In tinea manus, in contrast, only slight correlation could be

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1 Lewis, G M , Montgomery, R M , and Hopper, M E Cutaneous Manifestations of Trichophyton Purpureum (Bang), Arch Dermat & Syph **37** 823 (May) 1938

2 Montgomery, R M , and Caspar, E Cutaneous Manifestations of the Fungi Causing Dermatophytosis and Onychomycosis, J A M A **128** 77 (May 12) 1945

3 Bumgarner, F E , and Burke, R C Superficial Mycoses of Veterans I Survey of 1,000 Veterans with Service Diagnosis of Dermatophytosis, Arch Dermat & Syph **60** 742 (Nov) 1949

easier to isolate than is T rubrum Additional evidence rests on correlation of types of lesions with etiologic agents In other words, if a patient presents a chronic hyperkeratotic lesion of the feet from which T rubrum has been isolated and a chronic hyperkeratotic lesion of the hand not yielding a culture, one may expect with a high degree of certainty that T rubrum is also the etiologic agent of the tinea manus

TABLE 3.—*Dermatophytosis and Cutaneous Moniliasis*

	Number of Patients	Total Number of Patients	Percentage
Patients with single sites of infection		183	42 6
Feet	130		
Toe nails	18		
Groin	18		
Hand	10		
Finger nails	1		
Buttocks	4		
Leg	1		
Trunk	1		
Patients with two sites of infection		179	41 7
Feet, nails	140		
Feet, groin	18		
Feet, hands	9		
Feet, finger nails	2		
Groin, finger nails	2		
Gro'n, perineum	1		
Groin, toe nails	1		
Toe nails, finger nails	6		
Patients with three sites of infection		33	7 7
Feet, nails, groin	18		
Feet, na ls, hand	7		
Feet, nails, finger nails	1		
Feet, hand, leg	1		
Feet, groin, perineum	1		
Feet, groin, upper trunk	1		
Hand, groin, neck	1		
Nails, groin, buttocks	3		
Patients with four sites of infection		21	5 0
Feet, nails, hand, finger nails	6		
Feet, nails, groin, axilla	2		
Feet, nails, groin, hand	2		
Feet, nails, hand, leg	4		
Feet, nails, leg, groin	1		
Feet, nails, abdomen, groin	1		
Feet, nails, groin, buttocks	4		
Groin, leg, arm, axilla	1		
Patients with generalized infection		13	3 0
Total		429	100

GENERALIZED DERMATOPHYTOSIS

Table 3 lists patients with verified dermatophytoses according to sites For 42 6 per cent (183 patients) there was evidence of one positive site, for 41 7 per cent (179 patients) of two positive sites, for 7 7 per cent (33 patients), of three positive sites, for 5 per cent (21 patients) of four positive sites, and in 3 per cent (13 patients), of five or more positive sites For the last-mentioned patients the infection was termed generalized 10 of the 13 patients were white, and 3 were

(84 6 per cent) of the cultures yielding T rubrum Three of the 4 cases of chronic hyperkeratotic scaling yielding T gypseum occurred in Negroes Several cases of palmar chronic hyperkeratotic scaling due to T gypseum, in both Negro and white patients, were also noted

The chronic papulovesiculosquamous type of lesion occurred in 18 per cent, or almost as frequently as did the chronic hyperkeratotic scaling type It was possible to make cultures from 54 4 per cent of the 68 positive cases Of these cultures, T gypseum was isolated in 75 7 per cent and T rubrum in the others

Bullous lesions ranked fourth (15 per cent) in incidence Cultures were isolated in 74 per cent of the cases, T gypseum being identified in

TABLE 1.—*Type of Lesion and Etiologic Agent in the Cases of Tinea Pedis*

	Chronic Interdigitous Lesions	Bullous Lesions	Chronic Papulovesicular Squamous Lesions	Subacute Lesions	Severe Chronic Hyperkeratotic Scaling Lesions	Chronic Hyperkeratotic Scaling Lesions	Total
Cases	150	54	68	14	4	70	360
Percentage of total	41 7	15	18 9	4 9	1	19 4	100
No cultured	72	40	37	8	3	26	186
Percentage cultured	48	74	54 4	57 1	75	37 1	51
No yielding T gypseum	39	40	28	7		4	118
Percentage yielding T gypseum	54 3	100	75 7	87 5		15 4	63
No yielding T rubrum	26		9	1		22	58
Percentage yielding T rubrum	36		24 3	12 5		84 6	31
No yielding E floccosum	1				3		4
Percentage yielding E floccosum	1 4				100		2
No yielding C albicans	6						6
Percentage yielding C albicans	8 3						3

each instance Combined infection with T rubrum was recorded in 2 instances

Only 14 (5 per cent) subacute lesions (mycosis plus secondary infection) were proved to be tineal Antibacterial treatment was administered to some patients before positive cultures were obtained Cultures were obtained in 57 1 per cent of the cases, T gypseum being identified in 87 5 per cent Subacute lesions were of vesicular or bullous origin

Severe chronic hyperkeratotic scaling was noted in only 4 cases (0 1 per cent), from 3 of which cultures yielded E floccosum It was necessary to reculture material from 2 of these cases before the organism was obtained

One may reason that it is possible to identify the etiologic agent by clinical examination alone in the case of bullous and severe chronic hyperkeratotic scaling lesions—that is, T gypseum in the first instance

5 T gypseum was identified as the etiologic agent in about two thirds of the cases of tinea pedis yielding cultures and in about 60 per cent of the cases of tinea unguium yielding cultures T rubrum was identified as the etiologic agent in two thirds of the cases of tinea cruris and tinea manus

6 Correlation of types of lesion with species of fungus has been most successful in cases of tinea pedis and tinea unguium Six types of lesions were noted in each

7 The search for multiple clinical types should be painstaking, since the detection of the type aids not only in ultimate eradication but also in the clinical identification of the etiologic agent

8 Statistics indicate that it is the etiologic agent rather than the type of lesion which influences the possibility of isolation T gypseum is easier to isolate than is T rubrum

Harvard University

1031 South Broadway

TYPE 2 Inverted V infection, with pronounced symmetry, little if any epithelial debris and dulness of the nails (particularly if hyperhidrosis is associated) Usually all the nails on one or both feet are involved T gypseum is isolated in the majority of cases

TYPE 3 Asymmetric infection, with epithelial debris, thickened nail plate, infected nail bed and involvement of from 1 to 10 nails If the nails are in the same stage of involvement and, if the nails, particularly those on the second to fifth digits, are dull, T gypseum is the organism most frequently isolated If the nails are in varying stages of involvement and retain some luster, T rubrum is the fungus most often isolated

TYPE 4 —Ragged, opaque, thick and crumbly nails Both T rubrum (in the majority of the cases) and T gypseum have been isolated from such nails Often various saprophytes are also present In 1 instance, mycelium and conidia of Hormodendrum were noted throughout the nail tissue Several plates were planted with scrapings from the nail, and T gypseum and Hormodendrum sp were both isolated

TYPE 5 Nail uninfected, separated from infected nail bed T gypseum was isolated in 1 case, while in 5 other cases the agent was not obtained This type of lesion was noted only on the hands

TYPE 6 —Transverse ridges in nails which are frequently dull or opaque, with a serous exudate at times and occasional paronychia This is the well known C albicans type of lesion

It was possible to culture the organism from toe nails in 33 per cent and from the finger nails in 56 per cent of the cases The figure given for the toe nails is lower than that obtained in similar studies by Lewis and Hopper, as communicated to one of us (R C B) Final results of the study disclosed that of the 429 patients having dermatophytosis or cutaneous moniliasis, 245, or 57 per cent, had some degree of involvement of the nails All these, with the exception of 18, showed concurrent involvement of the feet or other parts of the body

Kittredge [7] stated that generalized involvement of all the nails was unusual and that the case he reported at the time was the seventh one to be reported Such occurrences, however, are not as unusual as the paucity of literature on the subject would indicate Three such cases, in all of which T rubrum was yielded, were uncovered among the veterans included in this study In addition, 11 cases of tinea unguium of all the toe nails due to T rubrum were recorded In 7 of these 11 cases the patient had acquired the infection in Alabama, Mississippi or Louisiana and presented not only type 3 involvement of all the nails

7 Kittredge, H E Onychomycosis Universalis Trichophytina et Epidermophyta Report of Seventh Case Thus Far Recorded in English, Arch Dermat & Syph **34** 398 (Sept) 1936

TABLE 1.—*Cases of Cutaneous Sarcoma*

No	Sex	Age, Yr	Duration	Race	Location	Metastases	Histology	Prognosis	Treatment
1	M	57	6 mo	W	Shoulder	+	Giant cell sarcoma	Died 3½ yr	Excision, amputation, roentgen irradiation, cyclotron irradiation
2	M	44	6 mo	W	Occiput	0	Fibrosarcoma	Living and well 2 yr	Excision
3	M	23	3 mo	W	Postauricular area	0	Fibrosarcoma	Living and well 7 yr	Excision
4	M	55	9 mo	W	Forehead	0	Fibrosarcoma	?	Excision
5	F	52	1 yr	N	Inguinal region	+	Mixed cell sarcoma	Died 1 yr	Excision, roentgen irradiation
6	M	15	6 mo	W	Scapular	0	Fibrosarcoma	Living and well 3 yr	Excision
7	M	70	4 mo	W	Thigh	+	Giant cell sarcoma	Died 1 yr	Excision
8	F	48	6 yr	W	Thigh	+	Fibrosarcoma	Died 6½ yr	Excision
9	M	46	5 mo	W	Thigh	+	Fibrosarcoma	Died 1 yr	None
10	M	45	4 yr	W	Arms, legs	0	Neurosarcoma (von Recklinghausen's disease) *	Died 10 yr *	None
11	F	26	1 yr	W	Thigh	0	Fibrosarcoma	Living and well 8 yr	Excision
12	M	26	1 yr	N	Shoulder	+	Fibrosarcoma	Died 1½ yr	Excision, roentgen irradiation (12,700r)
13	M	77	?	W	Preauricular area	0	Fibrosarcoma	Died 2 yr *	Excision
14	F	47	1 yr	W	Thigh	+	Rhabdomyosarcoma	Died 2½ yr	Disarticulation
15	F	28	4 yr	W	Popliteal space	+	Fibrosarcoma	Died 4 yr	Excision
16	M	62	2 yr	N	Arm	+	Fibrosarcoma	Died 2 yr	None
17	M	56	15 mo	W	Scapular	0	Fibrosarcoma	Living and well 2 yr	Excision
18	F	49	5 yr	W	Thigh	0	Neurosarcoma	Living and well 6½ yr	Excision
19	F	32	3 mo	W	Abdomen	0	Angiosarcoma	Living and well 9 mo	Excision
20	M	63	20 yr	W	Groin	+	Myxosarcoma	Died 22 yr	Excision, roentgen irradiation
21	M	39	1 yr	W	Foot	+	Fibrosarcoma	Died 2 yr	Excision
22	M	43	19 yr	W	Buttock	+	Fibrosarcoma	Died 20 yr	Excision, roentgen irradiation, phosphorus^{32} irradiation
23	M	67	2 yr	W	Back	+	Fibrosarcoma	Living, with recurrence 7 yr	Excision, roentgen irradiation
24	F	42	3 mo	W	Thigh	0	Fibrosarcoma	Living and well 10 yr	Amputation
25	F	8	2 yr	W	Face	+	Angiosarcoma	Died 3 yr	Excision, roentgen irradiation
26	M	1½	1 yr	W	Axilla	0	Angiosarcoma	?	Radium therapy
27	F	80	1 mo	W	Lip	0	Fibrosarcoma	?	Curettage and desiccation
28	F	37	4 mo	W	Arm, thigh	0	Fibrosarcoma	?	Curettage and desiccation

* The patient died of causes other than sarcoma

Three definite and distinct types of lesions were observed in tinea manus a chronic hyperkeratotic scaling, most frequently involving the palms and ventral surfaces of the fingers, a chronic papulovesiculosquamous eruption, which may involve the palm but which most frequently manifests itself on the dorsum of the hand and on the wrist, and a bullous type involving the palmar areas

The chronic hyperkeratotic scaling type has been observed most frequently, it was seen in 34 (65 4 per cent) of the total of 52 cases of different types of lesions Scaling is variable but usually fine and branny It was expected that T rubrum would always be isolated from this type, particularly since that was the general rule with chronic hyperkeratotic lesions of the feet However, of the 19 cases in which cultures were obtained only 14 (73 7 per cent) yielded T rubrum, the cultures in the other 5 (2 Negroes and 3 white patients) having yielded T gypseum (table 2)

TABLE 2.—*Type of Lesion and Etiologic Agent in Cases of Tinea Manus*

	Chronic Hyperkeratotic Scaling Lesions	Chronic Papulovesiculosquamous Lesions	Bullous Lesions	Not Listed	Total
Cases	34	12	1	5	52*
Percentage of total	65 4	23 8	1 9	9 6	100
Number cultured	19	9	1	5	32
Percentage cultured	55 9	75 0	100	60 0	61 5
Trichophyton gypseum	5	4	1	1	11
Percentage of T gypseum	26 3	44 4	100	33 3	34 3
Trichophyton rubrum	14	5	0	2	21
Percentage of T rubrum	73 7	55 5	0	66 6	65 7

* Four cases with both chronic hyperkeratotic scaling and chronic papulovesicular squamous lesions were observed

Chronic papulovesicular squamous lesions of the dorsum of the hand and wrist were observed in 12 cases In 9 of these, cultures were obtained In 4 the organism was identified as T gypseum and in 5 as T rubrum Several patients with this type of lesion of the hands had generalized dermatophytosis as well The bullous type of tinea manus was observed only once, on the thenar and hypothenar eminences of the left hand of a 26 year old Negro He also had bullous lesions of the feet T gypseum was identified from cultures of both areas

Of the 32 cultures made in cases of tinea manus, in 21, or 65 7 per cent, T rubrum was identified We believe that the greater part of the 44 per cent of uncultured chronic hyperkeratotic scaling lesions and of the 25 per cent of uncultured chronic papulovesicular squamous lesions were probably due to T rubrum This belief rests, in part, on evidence presented in table 1 and table 2, which indicates that T gypseum is

Table 4 outlines the differential points between sarcoma and epithelioma The most important features may be briefly mentioned Of the cases of sarcoma, 35 8 per cent occur in the precancer age The most common locations for sarcoma are on the extremities and the trunk, areas comparatively infrequently involved by epithelioma The massive growth and necrosis usually make the differentiation obvious Sarcoma is more frequent in Negroes than is epithelioma, and this may be of importance in some cases Sarcoma usually grows more rapidly than epithelioma The lesions of both sarcoma and epithelioma are usually single but may be multiple in either case Sarcoma often develops in

TABLE 3.—*Preoperative Diagnosis in 18 Cases of Sarcoma Involving the Skin*

Diagnosis	Cases	Diagnosis	Cases
Epithelioma	4	Hernia	1
Squamous cell	2	Gout	1
Basal cell	2	Polyarthritis	1
Sarcoma	3	Draining sinus tract	1
"Infectious granuloma"	2	Fibroma	1
Infected wound	1	Granuloma pyogenicum	1
Sebaceous cyst	1	Cutaneous tuberculosis	1

TABLE 4.—*Differential Diagnosis Between Sarcoma and Epithelioma*

Differential Point	Sarcoma	Epithelioma
Age	35 per cent less than 40	Usually over 40
Location	Trunk and lower extremities	Face and dorsa of hands
Clinical picture	Massive overgrowth	Ulceration
Negroes	More frequent	Less frequent
Growth	More rapid	Slower
Onset	Cutaneous or subcutaneous	Cutaneous
Surgical findings (gross)	Necrosis, greater spread than expected	Nodular and ulcerative
Metastases	Common	Comparatively infrequent
Lymph node involvement in presence of metastases	Infrequent	Probably always

the subcutaneous tissue, although it commonly appears in the true skin originally

While simple inspection and palpation may not establish the correct diagnosis, two features are found at surgical intervention that give one invaluable clues to the true nature of the neoplasm Even in small size, sarcoma extends more deeply than one would expect epithelioma of the same apparent size to do and second necrosis is present These features have been of great importance in this series

ETIOLOGY AND INCIDENCE

Obviously, the cause of sarcoma is unknown However, there are certain known factors of interest For instance certain precarcinomatous lesions may also be presarcomatous In this group might be included

Negroes Since white persons constituted two thirds of the total number studied, incidence by ratio was about the same for white persons as for Negroes

Cultures were isolated from 10 of the patients T rubrum was obtained from 8 white patients and T gypseum from 1 Negro and 1 white person Since T rubrum is more difficult to isolate than is T gypseum, one may assume that T rubrum is the cause of more than 80 per cent of the cases of generalized dermatophytosis

The most extensive case observed by us was that of R T, a 28 year old machinist, who stated that he had incurred the infection four years previously while he had been in the Navy The condition had remained chronic since that time and had gradually spread to cover three fourths of the body Both hands and feet showed chronic hyperkeratotic scaling of the palmer and plantar surfaces All toe nails and finger nails were infected Lesions of the chronic papulovesiculosquamous type extended from the area of the groin over the abdomen and buttocks and down the inner aspects of the thighs almost to the knees Similar lesions covered the forearms, the shoulders, the upper portion of the trunk and the neck and even extended onto the scalp T rubrum was isolated from several areas

TABLE 4.—*Sites of Generalized Tineal Infections*

Total Number of Patients	13
Total Number of Sites	95
Average Number of Sites per Patient	7 3

Site	Number of Patients	Site	Number of Patients
Feet	12	Finger nails	5
Groin	11	Abdomen	4
Buttocks	9	Scalp	4
Hands	9	Axilla	4
Toe nails	8	Concha of ear	4
Upper part of trunk	8	Arm	3
Legs	7	Face	1
Neck	6		

SUMMARY

1 Of the various clinical types of dermatophytosis, tinea pedis ranked first in incidence, followed in order by tinea unguium, tinea cruris, tinea manus and generalized tinea

2 Multiple clinical types of dermatophytosis were noted in more than half the patients with verified infections

3 Chronic hyperkeratotic scaling is recognized as being the most frequent type of tinea manus, occurring in about 66 per cent of the verified cases

4 Infected toe nails occurred in 60 per cent of the cases of tinea pedis In only 18 of the 245 cases of tinea unguium was there no clinical or laboratory evidence of concurrent dermatophytosis

regarding the importance or the lack of importance of trauma in initiating malignant changes Five more cases will not settle these arguments

There were 17 men and 11 women in this series However, in other reported studies there does not seem to be any significant difference in sex incidence

Twenty-five of the patients were white, the other 3 were Negroes Apparently, the Negro does not possess immunity from sarcoma parelleling his comparative freedom from certain other types of cancer, including basal cell epithelioma Furthermore, all 3 Negroes died of their sarcoma in an average of eighteen months The longest survival in a Negro in this group was two years This is a much shorter period of survival than the average for the entire series (5 35 years)

The age at the time of onset is given in table 5 This demonstrates that no age group is exempt The youngest patient was 1½ years of age, the oldest, 80 years of age Thirty-five and seven-tenths per cent of the patients were less than 40 years old the so-called precancer age

TABLE 5.—*Age at Onset of Sarcoma*

Years	Cases	Years	Cases
0 to 10	2	41 to 50	8
11 to 20	1	51 to 60	4
21 to 30	4	61 to 70	4
31 to 40	3	71 to 80	2

The 6 personally observed cases were culled from about 9,000 dermatologic cases, an incidence of 1 in 1,500 However, this incidence seems high, as I do not recall seeing sarcoma in any other group of dermatologic patients that have been under my care According to Eller,[5] primary sarcoma of the skin accounts for only 5 to 6 per cent of cases of all types of sarcoma occurring in the human body

PATHOLOGY

It is not the purpose of this paper to reiterate the well established criteria for the histologic diagnosis of sarcoma However it should be realized that despite clearcut textbook descriptions it is often difficult to establish the diagnosis of sarcoma For instance, MacKee,[3] as previously stated, claimed that the lesions arising in areas of radiodermatitis that have been diagnosed as sarcoma by general pathologists are in reality spindle cell epithelioma Montgomery [6] stated that most so-called

5 Eller, J J Tumors of the Skin Benign and Malignant, 1939, Lea & Febiger, Philadelphia, p 434

6 Montgomery, H Epithelioma of the Arm Simulating Endothelioma Sarcoma and Sporotrichosis Two Unusual Cases, M Clin North America **19** 605 (Sept) 1935

SARCOMA INVOLVING THE SKIN

ERVIN EPSTEIN, M D
OAKLAND, CALIF

TRADITIONALLY tumors have been divided into those of ectodermal and those of mesodermal origin The malignant neoplasms have been similarly divided into carcinoma, including melanoma, and sarcoma However, this classification is not completely satisfactory, since in some cases epithelioma, especially melanoma, reacts in the body in the same highly malignant manner as sarcoma Furthermore, in some cases sarcoma—in many of the cases neurosarcoma—is actually of ectodermal origin However, common usage makes this classification the most workable at this time

A voluminous literature has developed around the problems presented by cases of cutaneous epithelioma and melanoma While sarcoma is not completely neglected, comparatively little can be found in dermatologic writings concerning it Beerman,[1] in his excellent review on tumors of the skin, did not find enough to enable him to consider sarcoma Yet the dermatologist is often called on to diagnose and eradicate the smaller sarcomatous lesions As will be demonstrated later, sarcoma is among the most difficult to diagnose in the field of cutaneous neoplasms Furthermore, as in the case of epithelioma, cure depends on early recognition of the growth and prompt, adequate therapy

MATERIAL

The statements made in this paper are based on a study of 28 patients with histologically proved sarcoma involving the skin Six of the patients were encountered in private practice The remainder were studied from records made available by cooperating physicians and hospitals [2] In this series all of the neoplasms except 1, diagnosed as rhabdomyosarcoma, are believed to have originated in the skin and its appendages Cases of special types of sarcoma, well recognized by

From the Departments of Dermatology, Highland-Alameda County Hospital, Oakland, and Mount Zion Hospital, San Francisco

1 Beerman, H Tumors of the Skin A Review of the Literature, Am J M Sc **211** 480 (April) 1946, **212** 479 (Oct) 1946

2 This includes Highland-Alameda County Hospital, Mount Zion Hospital, Oakland Veterans Administration Hospital, Drs Norman N Epstein, Herman V Allington, J O Smith, Franklin I Harris, John Sampson and Allan Cohen

combined This is in contrast to the statements of Stewart and Copeland [8] and of Cutler, Buschke and Cantril,[9] who expressed the belief that soft tissue sarcoma is in most cases neurosarcoma In only 2 cases of this series was there evidence of associated von Recklinghausen's disease or of a tumor of a nerve trunk or of an unusual amount of nerve tissue in the sarcoma

Autopsies were performed in 9 cases Metastatic lesions were demonstrated in all 9 and, furthermore, the cell type of the metastases was identical with that found in the primary cutaneous tumor Death was due to cachexia or to terminal incidents, such as bronchopneumonia or nephritis The locations of the metastatic lesions are listed in table 7 This table indicates that metastases occurred most frequently in the lungs and the pleura, followed by the bones, the skin, the lymph nodes and the liver Autopsies revealed involvement of the deep lymph nodes more often than one would expect on clinical examination, suggesting that dissemination may occur through the lymphatic channels as well as through the blood stream

TABLE 7.—*Locations of Metastases Observed in 9 Autopsies*

Location	Cases	Location	Cases
Lungs and pleura	8	Heart	1
Skin	4	Kidney	1
Lymph nodes	4	Spleen	1
Bones	4	Peritoneum	1
Endocrine glands (adrenals, pancreas, pituitary)	3	Omentum	1
		Gallbladder	1
Liver	3	Subcutaneous tissue	1

PROGNOSIS AND TREATMENT

Obviously, therapy is imperative in this highly malignant condition In 13 of 24 cases in which there was a follow-up period of nine months or more, the patient had already died of metastases at the time of the last observation This is a mortality rate of 54.2 per cent Undoubtedly, this percentage would increase with more prolonged observation Two patients died of other causes, and their deaths are not included as resulting from sarcoma In these 13 cases the average period from the onset of symptoms to death was 5.4 years In the 11 cases in which the patient is still living or has died from other causes the average survival is 5.3 years The total for the entire group was 5.35 years

8 Stewart, F. W., and Copeland, M. M. Neurogenic Sarcoma, Am. J. Cancer **15**: 1235 (July) 1931

9 Cutler, M., Buschke, F., and Cantril, S. T. Cancer: Its Diagnosis and Treatment, Philadelphia: W. B. Saunders Company, 1938, pp. 659-666

dermatologists, as Kaposi's sarcoma and lymphosarcoma, were not included in this study Table 1 presents the 28 cases included in the series

CLINICAL PICTURE

Sarcoma develops in the skin or the subcutaneous tissue as a small nodule If superficially located, it grossly resembles epithelioma Growth may be rapid or slow, although the former is more common The nodule develops to form a mass which becomes elevated, discolored (usually purplish) and later necrotic and ulcerated Bleeding is common Later, the necrotic ulcer becomes fungating and granulomatous Involvement of regional lymph nodes is comparatively infrequent, this having been noted clinically in only 2 cases (7 1 per cent)

Only a single tumor was present in 24 cases (86 per cent) Multiple tumors were found in the other 4 Table 2 gives the location of these tumors There were 61 lesions in the 28 patients The most important finding is that in 39 4 per cent of the cases the lower extremities were

TABLE 2.—*Location of Tumors in this Series*

Location	Cases
Head	6
Trunk	10
Upper extremities	3
Lower extremities	11

involved In 35 8 per cent the trunk was affected Sarcoma was noted on the thighs in 28 6 per cent Epithelioma is definitely unusual in these locations

CLINICAL DIAGNOSIS

Sarcoma is easily diagnosed from its clinical appearance when it has become a massive purplish tumor with necrosis, ulceration and fungating overgrowth However, in no instance in this series was the clinical diagnosis suggested on simple inspection of a small growth The clinical diagnoses in 18 cases in which a tentative diagnosis was offered prior to surgical intervention are given in table 3 In the 3 instances in which the tumor was correctly diagnosed, the lesion was far advanced In the personally observed 6 cases the diagnosis was sarcoma in 1 (a large necrotic mass), squamous cell epithelioma in 1, basal cell epithelioma in 2, granuloma pyogenicum in 1 and fibroma in 1 The only other common diagnosis in the other 22 cases was infectious granuloma, including cutaneous tuberculosis, in 3 cases Therefore, the most important differential problem is that of epithelioma The coincident, adjacent occurrence of epithelioma and sarcoma in 2 cases further complicated the problem of diagnosis

well without evidence of recurrence or metastases after an average survival period of 2 75 years One patient succumbed to metastases three years postoperatively There was no opportunity to make follow-up studies on the sixth patient [10]

Amputation does not offer a better prognosis than simple excision, provided, of course, that the latter is adequately performed In addition, excision avoids the permanent disability that follows amputation For instance, patient 11 presented a large nodular fibrosarcoma of the thigh of one year's duration The histologic section was classified as grade 2 The lesion was completely excised, and the patient is living and well eight years later Of perhaps even greater importance, she has been able to lead a normal life, having had two successful pregnancies since and being able to raise her children

Irradiation may cause regression of the tumor, but there is no evidence that it is curative Most authorities agree that these types of sarcoma are radioresistant Radiation therapy should not be used as a substitute for surgical removal nor can postoperative radiation act as a safety mechanism to compensate for inadequate excision

SUMMARY

A study of 28 patients with histologically proved sarcoma involving the skin is presented

The lesions start as small nodules, which become massive, necrotic, ulcerated, fungating tumors

Epithelioma is the most important of the lesions to be differentiated from sarcoma and the most difficult to differentiate

Precarcinomatous lesions may be presarcomatous, and patients with sarcoma may have associated carcinoma

To diagnose sarcoma on purely histologic grounds is difficult and may be fallacious The histologic observations should be correlated with the clinical findings and course

The earlier treatment is instituted, the better the prognosis The mortality was almost 250 per cent greater in the group receiving treatment after six months than in those being cared for less than six months from the onset of the tumor

Adequate excision is apparently the treatment of choice

447 Twenty-Ninth Street

10 These statistics must be modified, as metastastic lesions developed in 1 other patient while this paper was in press See footnote 4a

lupus vulgaris, xeroderma pigmentosum and radiodermatitis MacKee[3] and others have stated that it is doubtful that sarcoma ever develops in areas of radiodermatitis While cases have been reported in which a lesion developing in such an area histologically resembled sarcoma, he felt that it was actually of epithelial origin In case 2 of this series a lesion diagnosed as sarcoma developed less than 1 inch (2 5 cm) from a lesion diagnosed as squamous cell epithelioma in an area of radiodermatitis The former was of greater duration than the latter, but both lesions were present at the same time and were excised in a single block dissection Histologically there was no resemblance between the two lesions After a study of special stains (Masson's, silver impregnation and phosphotungstic acid) Biskind[4] felt that the sarcomatous lesion was of mesodermal origin[4a] In case 13 three lesions were removed from the face of a 77 year old man at the same time Histopathologic examination revealed that one lesion was basal cell epithelioma, one was mixed cell epithelioma and the third sarcoma

Six apparently unrelated conditions occurred concurrently with sarcoma in this series Four psoriasis, lupus erythematosus, polyarthritis and cholelithiasis—were obviously coincidental, and each occurred in 1 case only Tuberculosis was noted twice Sarcoma was associated with carcinoma in 3 instances This is 10 7 per cent of the entire series but is 16 6 per cent of the patients over 40 years of age, i e , in the cancer age

The evidence presented in the two previous paragraphs causes one to speculate whether the factor that leads to the development of sarcoma is not the same as that which leads to carcinomatous degeneration Apparently there is in certain patients and certain lesions a tendency toward malignant changes, and the malignant cells may be of epidermal or mesodermal origin

Trauma seemed to be important in the development of sarcoma in 5 cases, 17 8 per cent In 4 cases the patient related the onset of the tumor to a severe traumatic incident involving the affected area These included a kick in the buttocks in a fight, a home accident, an automobile accident and an industrial accident In the fifth case, apparently a recurrent low grade sarcoma of twenty years' duration became actively malignant, the growth was accelerated and death occurred two years after an automobile accident The literature is filled with arguments

3 MacKee, G M X-Rays and Radium in the Treatment of Diseases of the Skin, ed 3, Philadelphia, Lea & Febiger, 1938, p 355

4 Biskind, G Personal communication to the author

4a According to a report received from Major Robert B Franklin, Medical Corps, United States Air Force, dated July 29, 1949, this patient was hospitalized because of metastases in the left pleura and the liver Such metastases are much more suggestive of sarcoma than of epithelioma

fragments of glass The fluorescent powder which lines tubes of this type is comprised of a calcined mixture of zinc oxide, manganese oxide, beryllium oxide and silica In these 4 patients the lacerations healed with production of excess fibrous tissue Two of the lesions, when first seen by physicians, were believed to be simple keloids All four lesions, on one or more occasions after initial healing, opened to discharge thick,

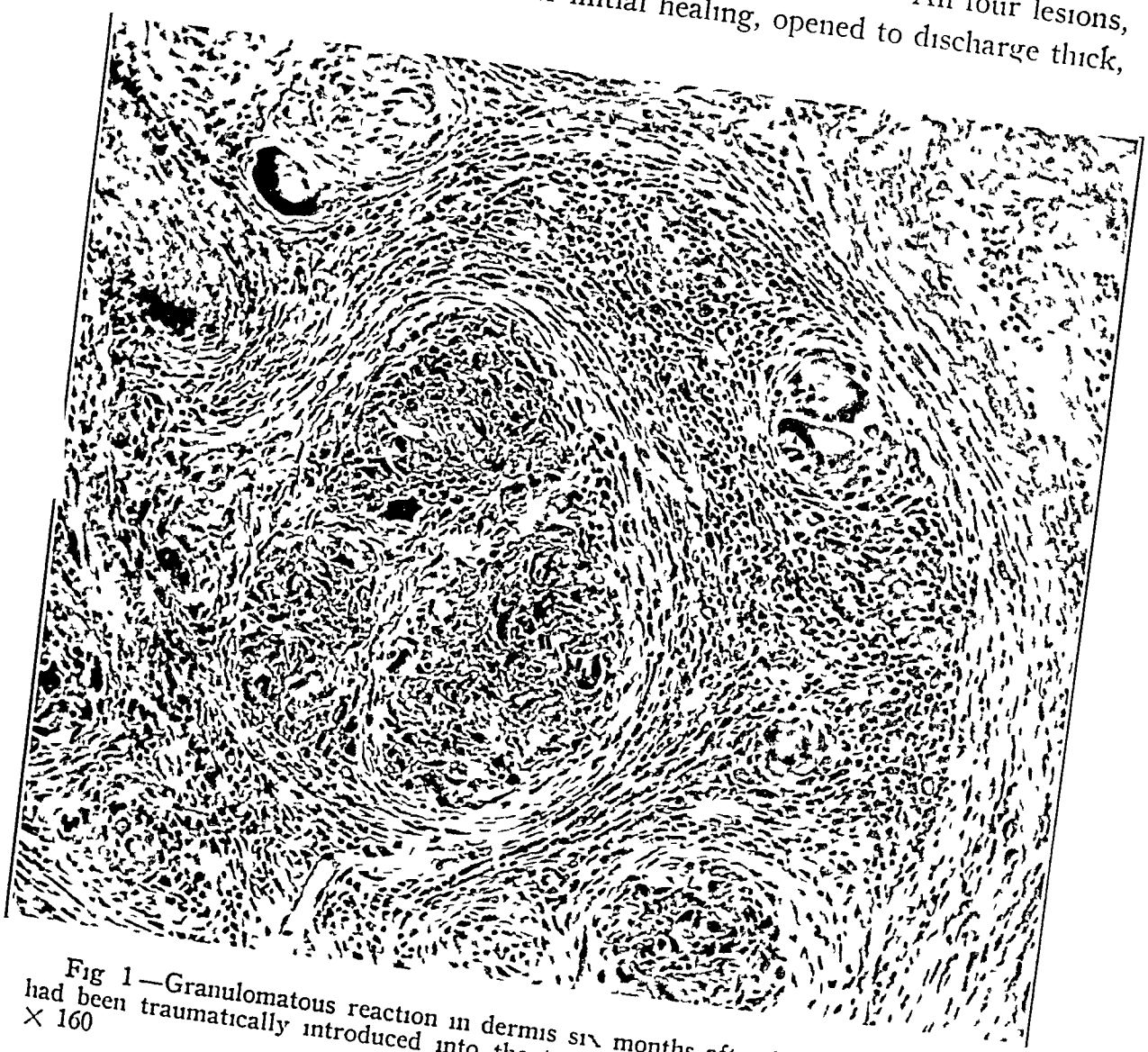


Fig 1—Granulomatous reaction in dermis six months after beryllium phosphor had been traumatically introduced into the tissues, hematoxylin and eosin stain, × 160

grayish white necrotic material The period from injury to excision varied from four months to nine years

A fifth patient discussed here was a young woman who worked at cutting metallic beryllium with a machine and had accidentally lacerated her finger during her work A granuloma developed, and this failed to heal over a period of four years, so that finally a complete excision of the lesion was made

cases of sarcoma of the extremities are actually cases of epithelioma Furthermore, it is often difficult to determine whether a lesion is a sarcoma or very cellular, nonencapsulated benign fibroma This is well illustrated by the case reported by Eller and Kest [7] Biopsy specimens were sent to a number of leading skin and tumor pathologists The following diagnoses were offered by these admitted experts D L Satenstein and D Wilbert Sachs—"small spindle cell sarcoma with hemorrhage", Emmerich von Ham "fibrosarcoma", Hamilton Montgomery—"angiosarcoma", Paul Klemperer—"fibrosarcoma", J Frank Fraser—"fibrosarcoma", Fred D Weidman "fibrosarcoma", Francis Carter Wood—"neurofibroma" In a study of cases presented before various dermatologic societies in this country it is obvious that this is not an unusual experience

This demonstrates the difficulty of accepting histologic observations as the only proof of the diagnosis of sarcoma It is a medical axiom that the laboratory results must be correlated with the clinical findings in all

TABLE 6—*Histologic Types of Sarcoma*

Type	Cases
Fibrosarcoma	18
Angiosarcoma	3
Giant cell sarcoma	2
Neurosarcoma	2
Mixed cell sarcoma	1
Rhabdomyosarcoma	1
Myxosarcoma	1

branches of medicine Therefore, it is suggested that the diagnosis of sarcoma must be based not only on the histopathologic aspects but on the clinical findings and on the course of the neoplasm as well

In this series the diagnoses were made by 12 different pathologists While any given histopathologic section was examined by more than one pathologist in only a few instances, the fact that so many pathologists were involved ruled out the possibility that this series was influenced unduly by personal factors on the part of the examiner Furthermore, the mortality of 54 2 per cent speaks eloquently for the obvious fact that, whatever criteria are employed, most of these cases were instances of highly malignant sarcoma

The histologic types of the tumors are given in table 6 The cases of giant cell sarcoma may be included in the group of cases of fibrosarcoma, so that the latter diagnosis was made in 71 5 per cent of the total number of cases of sarcoma of the skin In other words, fibrosarcoma occurred three times as frequently in the skin as did all the other forms of sarcoma

7 Eller, J J, and Kest, L H Sarcoma Arising in an Organized Hematoma Resulting from a Single Trauma, Arch Dermat & Syph **43** 813 (May) 1941

of Boeck's sarcoid in which caseous necrosis does occur [4] There was amorphous, slightly eosinophilic, granular material, and at one point a small, highly refractile mass of foreign material was present Around the necrotic center there were large mononuclear cells, some of which were polyhedral while others were spindle-shaped These cells had large reticular nuclei, so that they resembled epithelioid cells The necrotic areas were surrounded by a zone of partially degenerated, elongated cells resembling fibroblasts, around which there was cellular

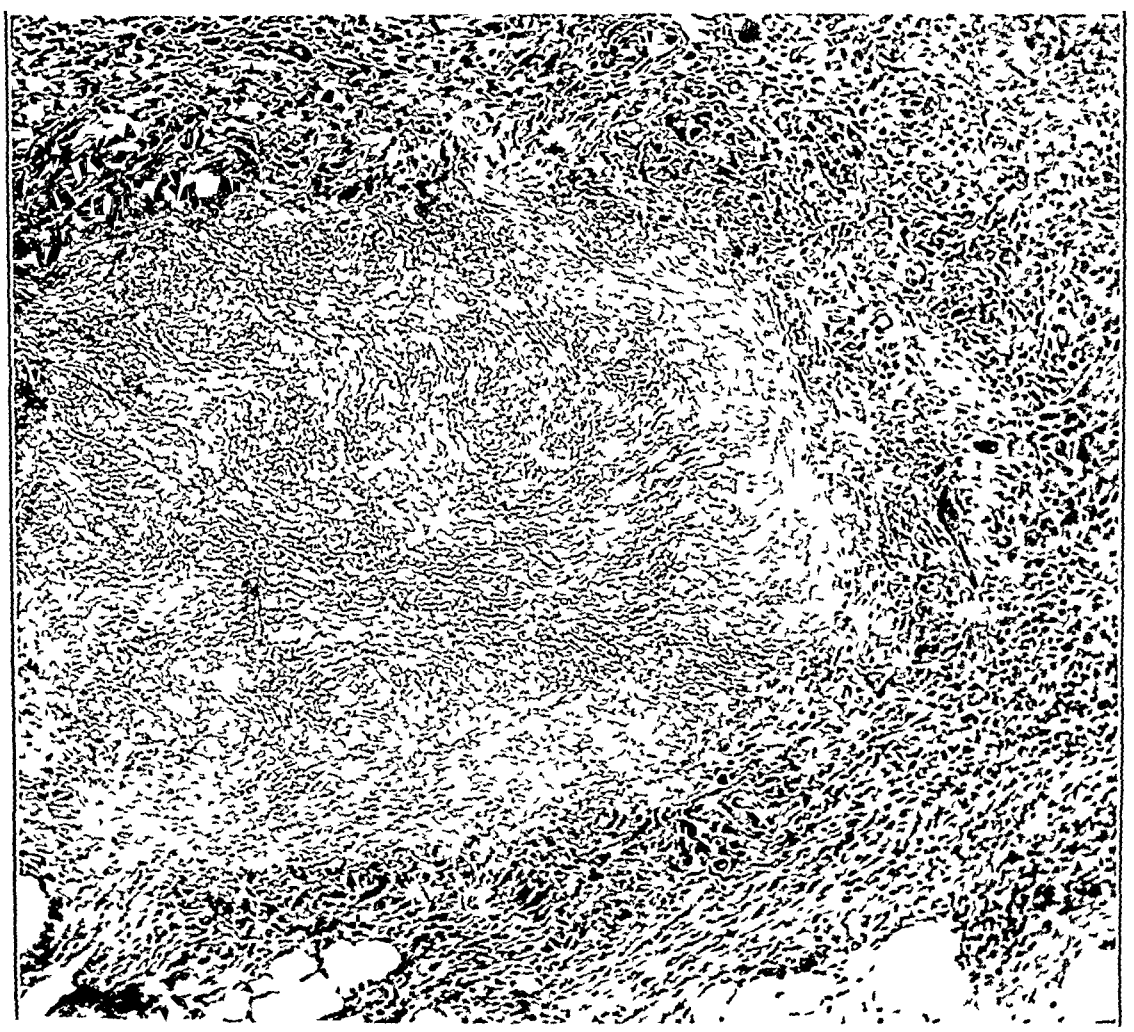


Fig 3—Area of necrosis of dermis four months after introduction of beryllium phosphor, hematoxylin and eosin stain, × 115

collagenous tissue infiltrated with large numbers of lymphocytes The remainder of the tissue was divided by relatively dense strands of connective tissue into nodules of varying sizes The nodules were comprised in most instances of relatively loosely arranged connective tissue, in which there were elongated and polygonal cells with large reticular nuclei, surrounded by elongated fibroblasts and a few lymphocytes The

4 Goldman, L Personal communication to the author

The longest life was twenty-two years, and the shortest in the fatal cases was one year after the appearance of the primary tumor

The earlier treatment is instituted, the better the prognosis If one employs a duration of six months as an arbitrary dividing line between early and delayed treatment, one finds that the mortality in the early-treated group was 30 per cent of the 10 patients receiving prompt attention On the other hand the mortality in 14 receiving treatment more than six months after the onset was 71 4 per cent While the number of cases studied may not be significant, these figures support the obvious thesis that the earlier adequate treatment is instituted, the better the prognosis It is to the credit of both the patients and the physicians that almost 35 per cent of the patients received treatment less than six months after the appearance of the tumor

Three patients were untreated throughout the course of their sarcoma All died, the average period of survival being 4 3 years However, this

TABLE 8—*Mortality with Each Type of Treatment*

Type of Treatment	Patients	Mortality
Excision	21	9 (42 7%)
Roentgen irradiation	7	6 (85 8%)
Amputation	3	2 (66 6%)
Curettage and electrodesiccation	2	0
Cyclotron irradiation	1	1 (100%)
Phosphorus ^{32} irradiation	1	1 (100%)
Radium irradiation	1	0
None	3	3 (100%)

comparatively favorable average is unduly influenced by the inclusion of a patient with a questionable diagnosis of low grade neurosarcoma This patient died ten years after the onset of his sarcoma, but death was due to an intercurrent tumor of the bladder diagnosed as carcinoma The average for the other 2 patients was 1 5 years, a figure which is probably closer to the true outlook for patients with untreated cutaneous sarcoma

It is difficult to compare different schemes of treatment because the prognosis depends on many factors, such as duration of the lesion prior to the onset of treatment, race, thoroughness of treatment and presence or absence of metastases Furthermore, a small series does not allow dogmatic statements Many patients received more than one form of treatment Table 8 shows the number of patients receiving each type of treatment and the number dying despite the approach utilized

It is important to note that more than 50 per cent of the patients treated by excision, with or without auxiliary measures, were still living at the time this study was conducted Furthermore, of 13 patients treated with excision alone, 7, or 53 8 per cent, survived Of 6 patients whom I personally treated by radical cautery excision, 4 are living and

moderate acanthosis, hyperkeratosis and parakeratosis The peripheral portions of the lesions were infiltrated by numerous lymphocytes, but within the lesion itself such cells were relatively few

The lesions from 3 other patients who had had phosphors embedded in their skin for periods of from one to four years before excision were similar to the one described The lesion from the woman who had had metallic beryllium embedded in her skin for a period of four years was also similar to the one described

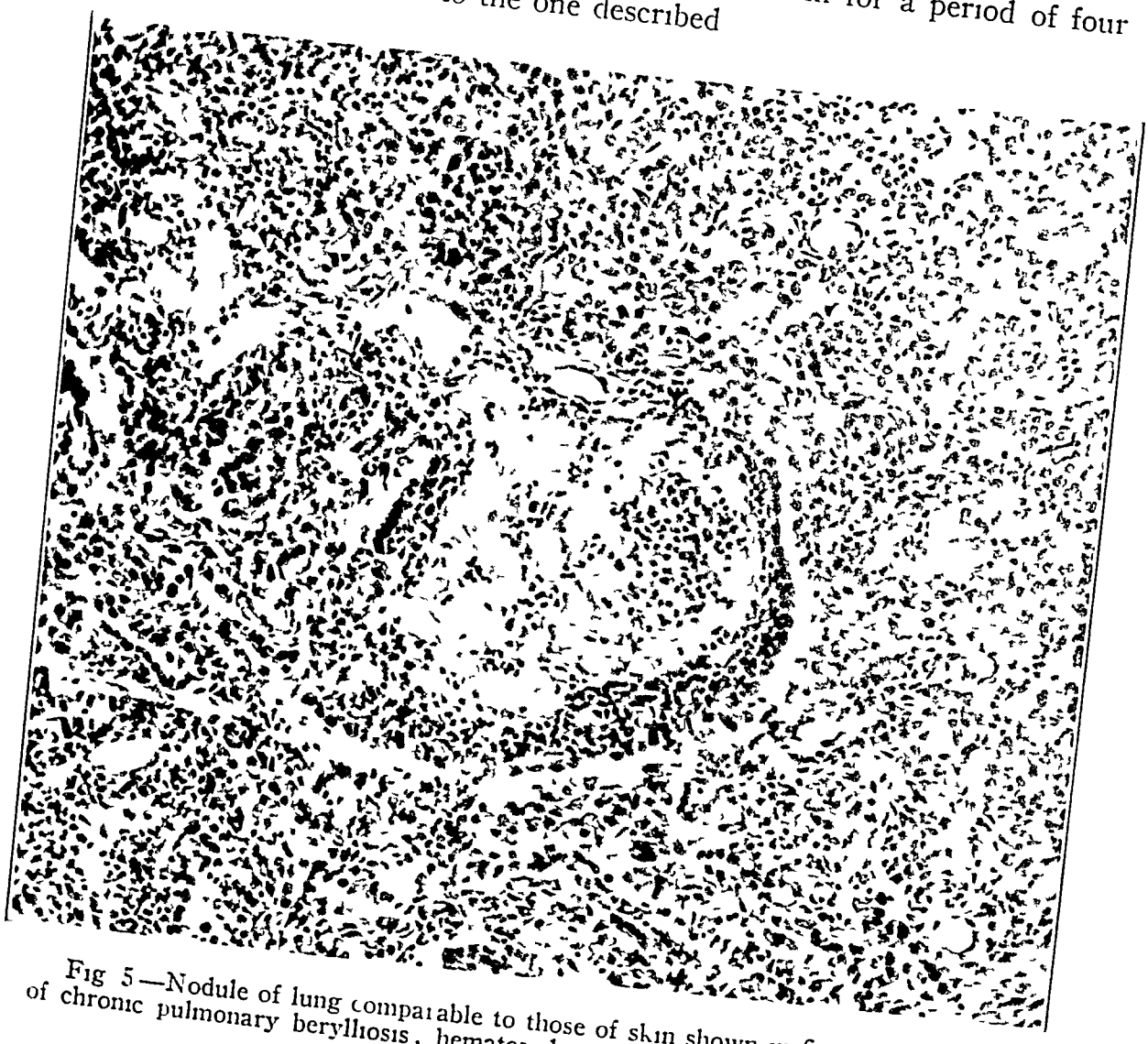


Fig 5—Nodule of lung comparable to those of skin shown in figure 4, in a case of chronic pulmonary berylliosis, hematoxylin and eosin stain, × 160

The lesion in the skin of the man who had had beryllium phosphor embedded at that site nine years before it was excised differed somewhat in degree of development from those the duration of which had been four years or less In the nine year lesion the general picture was one of dense, relatively acellular collagen in which were numerous small nodules comprised of large cells The latter were for the most part compactly arranged, with poorly defined pale cytoplasm and large vesicular nuclei Occasional small multinucleated cells which resembled

BERYLLIUM GRANULOMAS OF THE SKIN

FRANK R DUTRA, M D
CINCINNATI

IN A RECENT paper, Grier, Nash and Freiman [1] have reviewed the literature relating to the effects which beryllium may have on the skin and subcutaneous tissues They recognized four distinct types of cutaneous reaction to beryllium Contact dermatitis occurs in persons working with soluble salts of beryllium, particularly beryllium fluoride or beryllium sulfate [2] Ulcers result when crystals of soluble beryllium salts become embedded in the tissues, these heal only after the crystals have been removed surgically or have been extruded spontaneously [2] In some patients suffering from chronic pulmonary berylliosis, granulomas of the skin occur, and these are similar to the granulomas which develop in the lungs [3] Grier and his co-workers have observed a fourth variety of cutaneous reaction to beryllium which they term "subcutaneous granuloma occurring in persons who cut themselves on fluorescent lamps"

Tissues received from 4 persons in whom subcutaneous granulomas developed after beryllium compounds had been traumatically introduced into the skin have been examined at the Kettering Laboratory We have also received tissues from an additional person in whom granulomatous inflammation of the subcutaneous tissues followed the introduction of metallic beryllium

CLINICAL DATA

The clinical data were essentially similar for all 5 patients In 4 the beryllium was embedded in the skin as the result of the accidental breaking of fluorescent lamp tubes and the puncturing of the skin by

This work was done under a contract with the Office of Naval Research

From the Kettering Laboratory of Applied Physiology, University of Cincinnati, College of Medicine

1 Grier, R S , Nash, P , and Freiman, D G Skin Lesions in Persons Exposed to Beryllium Compounds, J Indust Hyg & Toxicol **30** 228-237, 1948

2 Van Ordstrand, H S , Hughes, R , De Nardi, J M , and Carmody, M G Beryllium Poisoning, J A M A **129** 1084-1090 (Dec 15) 1945

3 Hardy, H L , and Tabershaw, I R Delayed Chemical Pneumonitis Occurring in Workers Exposed to Beryllium Compounds, J Indust Hyg & Toxicol **28** 197-211, 1946 Pyre, J , and Oatway, W H , Jr Beryllium Granulomatosis, Alias Miliary Sarcoid, Salem Sarcoid, Miliary Sarcoidosis, Chronic Beryllium Poisoning, or Delayed Chemical Pneumonitis, Arizona Med **4** 21-29, 1947

tubercle bacilli The beryllium lesion can be differentiated from Boeck's sarcoid by the presence of caseous areas and by the large number of lymphocytes scattered throughout, particularly in the periphery of the lesion It is probable that tertiary syphilis might simulate the cutaneous beryllium granuloma, and the differentiation would depend on the demonstration of treponemas and the failure to demonstrate beryllium Nodular leprosy and certain cutaneous fungous diseases would present only minor difficulties of differentiation

The treatment of cutaneous and subcutaneous granulomas which follow the introduction of beryllium or its compounds has been successful in the 5 cases reported here only when the tissues containing the foreign material have been completely excised Before excision, in each case, the lesion was marked by excessive formation of scar tissue and repeated episodes of discharge of the wound, followed by temporary healing

SUMMARY

Five cases of chronic granulomatous inflammation of the skin and subcutaneous tissues following the introduction of beryllium or beryllium compounds are presented

The histologic relationship of the granulomas of the skin and similar granulomas which occur in the lungs of persons who have inhaled beryllium-containing dusts in industry is described

Cure followed excision of the lesions in all cases

HISTOPATHOLOGIC OBSERVATIONS

The tissues which were excised four months after the phosphor-containing beryllium oxide had been introduced into them were found to be the site of a granulomatous reaction in which there were areas of



Fig 2.—Focal necrosis and granulomatous inflammation of dermis four years after metallic beryllium had been introduced into the tissues, hematoxylin and eosin stain, × 160

necrosis The necrotic areas involved the dermis and subcutaneous tissues, and they were not unlike the areas of caseation in tuberculosis, they were, however, much more extensive than those in the rare cases

ment is most applicable to the matured "polar" lesions, it is least true with reference to the macular lesions It will be instructive, however, and of great practical value, for one to try to apply this observation to the simple, flat, usually hypopigmented macular lesions of the disease

Bacterioscopy The bacillary content of the tissue fluid at the border of the lesion is perhaps the most useful criterion If material obtained by Wade's "scraped incision" method [3] (which is still inaccurately but concisely called a "snip" in Hawaii) shows abundant bacilli, the lesion is probably lepromatous, if it shows few or none, the lesion is probably tuberculoid, if it shows moderate numbers, the nature of the lesion has not yet been determined, and the case, though not classifiable as either lepromatous or tuberculoid in type, may be said to be in the indeterminate group, at least so far as bacterioscopic evidence is concerned

The examination for bacilli may also be made on sections of tissue, preferably with the aid of Fite's formaldehyde modification [4] of the Ziehl-Neelsen stain More sensitive methods of searching for bacilli (as described by de Souza-Araujo [5]) are useful in diagnosis but not particularly helpful in differentiating the types

Neurologic Findings Concomitant and coextensive nerve damage is probably of almost equal importance in classifying the case as tuberculoid Demonstrable anesthesia which is identical in extent with the hypopigmentation is strong evidence that the lesion is not lepromatous but maculoanesthetic, i e, tuberculoid in immunologic type if not (yet) in histologic structure, for it is in this type that the neurolytic defensive reaction to the bacillus occurs In this connection, it is often forgotten even by experienced workers that anesthesia in leprosy is apt to occur in a dissociated pattern, e g, anesthesia to cold or heat or to both, with unimpaired sensitivity to light touch and to pinprick, is commonly found in early lesions In lesions manifesting no apparent anesthesia, the histamine test of Rodriguez and Plantilla [6] may be employed (in patients with light-colored skins) to detect lesser degrees of nerve dam-

3 Wade, H W Bacteriological Examination in Leprosy, Leprosy Rev **6** 54 (April) 1935

4 Fite, G L The Staining of Acid-Fast Bacilli in Paraffin Sections, Am J Path **14** 491 (July) 1938, The Fuchsin-Formaldehyde Method of Staining Acid-Fast Bacilli in Paraffin Sections, J Lab & Clin Med **25** 743 (April) 1940 Tilden, I L, and Tanaka, M Fite's Fuchsin-Formaldehyde Method for Acid-Fast Bacilli Applied to Frozen Sections, Am J Clin Path **15** 95 (Nov) 1945

5 de Souza-Araujo, H C Clamp Method to Obtain Cutaneous Lymph in the Diagnosis of Leprosy, Leprosy Rev **18** 44 (April-July) 1947

6 Rodriguez, J, and Plantilla, F C The Histamine Test as an Aid in the Diagnosis of Early Leprosy, Philippine J Sc **46**·123 (Sept) 1931 Internat J Leprosy **1** 49 (Jan) 1933

entire nodules were surrounded by relatively dense connective tissue in circumferential arrangement In the centers of some of the nodules and in the peripheral portions of others were multinucleated giant cells of the Langhans type, some of which were as small as 20 microns in diameter, while others were as much as 200 microns in diameter Some of these giant cells had within their cytoplasm small masses of highly refractile substance, but in none were there inclusion bodies of the type described by Schaumann [5] or of the type described by Wolbach [6]



Fig 4—Marked fibrosis of individual nodules in granuloma nine years after beryllium phosphor was introduced into dermis, hematoxylin and eosin stain, × 160

The lesions occupied the dermis and the uppermost portion of the subcutaneous tissues The epidermis was intact, and there were

5 Schaumann, J On the Nature of Certain Peculiar Corpuscles Present in the Tissue of Lymphogranulomatosis Benigna, Acta med Scandinav **106** 239-253, 1941

6 Wolbach, S B A New Type of Cell Inclusion, not Parasitic, Associated with Disseminated Granulomatous Lesions, J M Research **24** 243-257, 1911

loid" in a larger series of similar lesions He often found it necessary to employ serial sections, however Ota and Sato,[13] in Japan, came independently to exactly the same conclusion in the same year

What is meant by "in some degree tuberculoid"? Not fully developed, noncaseating, epithelioid cell tubercles, to be sure In general, the designation refers to an infiltrate of rather sharply focal arrangement, composed of both lymphocytes and epithelioid cells, which may or may not be arranged in the pattern of definite tubercles Diffuseness or vague margination of the infiltrate and scarcity of lymphocytes are both suggestive of the lepromatous form of the disease

THE INDETERMINATE GROUP

If bacterioscopic, neurologic, clinical and histologic changes are inconclusive or inconsistent, the problem is a more difficult one, it may indeed be incapable of solution for the time being The South American dermatologists, perhaps impatient at the postponement of an exact diagnosis, have urged the establishment of a third "type" or "form" of leprosy to include all such cases they suggested calling them *incaracterístico* (uncharacteristic) At the Fifth International Congress for Leprosy, in April 1948, the words "indeterminate" and "group" were agreed on the former because it permitted the use of the same initial letter, *I,* in Portuguese, Spanish, French and English, and the latter to indicate that this term designated, not a third type of leprosy, but only a group of cases, defined largely by their lack of definitive characteristics It has been shown that such cases may remain in this neutral status for a variable period, at the end of which they will heal, become lepromatous or become tuberculoid

In addition to the differentiating criteria which have been discussed, there is one more point, regarded by some workers as the most informative and important of all, which presents so many ramifications that I shall discuss it under a separate heading

LEPROMIN (FERNÁNDEZ AND MITSUDA) REACTIONS

Kensuke Mitsuda reported in 1916[14] that the intracutaneous injection of a small amount of a phenolized, boiled suspension of finely divided lepromatous granulation tissue (a mixture of dead Mycobacterium leprae and human tissue) would produce a slowly developing often ulcerated papule in the great majority of patients with the "maculoanesthetic" (i e, tuberculoid) form of leprosy, as well as in many

13 Ota, M, and Sato, S Tuberculoid Changes in Leprosy Internat J Leprosy 5:199 (April-June) 1937

14 (*a*) Mitsuda, K, in discussion in Jap J Dermat **16**:513 (June) 1916, (*b*) cited by Hayashi, F Mitsuda's Skin Reaction in Leprosy, Internat J Leprosy **1** 31 (Jan) 1933

Langhans' cells were present There was a large number of lymphocytes scattered throughout these nodules, interspersed between the large cells Many of the nodules had dense collections of numerous lymphocytes in their peripheral portions, and practically all of the nodules were surrounded by collagen which contained only a few small connective tissue cells In some places this collagen was hyalinized

In 3 of the 5 cases sufficient amounts of tissue were available to permit chemical analysis The tissues were analyzed for beryllium by the method of Cholak and Hubbard,[7] and small quantities of beryllium were recovered in 2 cases but could not be recovered in the third

COMMENT

The evidence which supports the opinion that beryllium is capable of producing fibrosis has been presented in a paper[8] in which 13 cases of chronic pulmonary berylliosis with fibrosis and granulomas are described Among 7 cases of acute pneumonitis due to the inhalation of fumes or dusts containing beryllium, there were organization of exudate and early fibrosis in 5, and the lesion progressed to the first stage of the formation of fibrous nodules in 3 Further support of the opinion that beryllium is capable of inducing fibrosis has come from experimental work in which the reactions induced by metals embedded in bone were studied[9] It was found that a certain alloy containing nickel, cobalt, chromium and molybdenum was innocuous, but that when beryllium was added to the alloy in the concentration of 1 6 per cent, granulation tissue formed at the site of the alloy and lymphocytes infiltrated the tissues

The diagnosis of beryllium granuloma of the skin can probably be made clinically when there is a history of beryllium or one of its compounds having been embedded in the skin Lacerations produced by glass from fluorescent lamp tubes are likely to lead to the development of beryllium granulomas, since beryllium oxide is a constituent of the phosphorescent powders used in making these tubes Tissues into which the material has been introduced will, over some months, show formation of excessive scar tissue, which occasionally opens and drains Biopsy of such tissues reveals lesions which could be confused with caseous tuberculosis or Boeck's sarcoid Differentiation rests on the presence of beryllium demonstrated by analytic methods, and on the absence of

7 Cholak, J, and Hubbard, D M Spectrographic Determination of Beryllium in Biological Material and in Air, Analyt Chem **20** 73-76, 1948

8 Dutra, F R The Pneumonitis and Granulomatosis Peculiar to Beryllium Workers, Am J Path **24** 1137-1166, 1948

9 Campbell, E H , Meirowsky, A , and Tompkins, V Studies on the Use of Metals in Surgery II Experiments in the Use of Ticonium in Cranial Repair, Ann Surg **116** 763-775, 1942

Fernandez,[17] in 1940, reported that the often observed tuberculin type of reaction to lepromin, reaching peak severity in forty-eight hours instead of the two to five weeks required for the Mitsuda reaction, could be correlated with the clinical form of the leprosy virtually as closely as could the latter Dharmendra and Lowe,[18] in 1943, showed that this response could be elicited regularly by injection of the purified protein, presumably the nucleoprotein, of the bacilli The injection of the crude antigen, on the other hand, generally produced relatively little effect until the bacilli had had time to break down and liberate this antigenic material It is highly probable, at all events, on the basis of this evidence and the analogy with some (though by no means all) forms of tuberculosis, that a positive lepromin test indicates acquired allergic hypersensitivity to the antigens of the leprosy bacillus, though this may have been acquired without infection by, or even contact with, the organism in question I know of no student of leprosy who believes that a strongly positive Mitsuda reaction can occur in a patient with low resistance to leprosy, or a negative or even a feeble reaction in one with high resistance The allergic response and the defensive one seem, in leprosy, inseparable

Hayashi[14b] and others showed that the Mitsuda reaction may be more pronounced in tuberculoid "macules" than in normal skin This observation was confirmed most recently by Davey[16] The reaction is apt to be stronger in elevated tuberculoid "macules" than in flat ones and is usually strongest in their borders A positive reaction is also occasionally found, according to Davey, in lepromatous macules, even when the normal skin outside the macule gives a negative reaction Dharmendra,[19] in a recent extensive review of the literature on the lepromin test, stated that he had not been able to confirm this observation, and my experience in Hawaii has been similar

SIMPLE (FLAT) MACULES VERSUS TUBERCULOID (ELEVATED) "MACULES"

I have discussed in some detail the features of the two types of flat macules, the lepromatous and the anesthetic, or simple The elevated or tuberculoid, "macules" present no such highly refined problem in differentiation, for in them the allergic hypersensitivity to Myco leprae is strongly and usually securely established The histologic changes which are almost invariably of the tuberculoid pattern, with

17 Fernandez, J M M The Early Reaction Induced by Lepromin, Internat J Leprosy 8 1 (Jan-March) 1940

18 Dharmendra and Lowe, J Studies of the Lepromin Test, Leprosy in India **15**.82 (April) 1943, Leprosy Rev **17** 9 (April) 1946

19 Dharmendra The Lepromin Test A Review, Leprosy Rev **18**.92 (Oct) 1947

"MACULES" OF LEPROSY

HARRY L ARNOLD Jr, M D
HONOLULU, HAWAII

THE WORD "macule" has long been used by students of leprosy in two quite different and yet overlapping senses Exceptionally, it has been used in the orthodox sense of a circumscribed, flat discoloration of the skin (usually hypopigmentation, and less often erythema), and in this use it is, oddly enough, usually qualified as either "lepromatous" or "simple" (or "anesthetic") or, more recently, "uncharacteristic" or "indeterminate"

The term has been much more commonly used, however, in a sense at once looser and more restricted, and certainly not at all orthodox Without any qualifying adjective, the word "macule" [1] has been used to designate any circumscribed, discolored (hypopigmented erythematous or both) cutaneous lesion, flat or elevated, in which (1) evidence of nerve damage (usually anesthesia) can be demonstrated and (2) bacilli are rare or absent When such a lesion is flat, it is often spoken of as a simple or an anesthetic macule, when it is elevated (and sometimes even when it is not), it is often called a tuberculoid 'macule"

There is, then, a morphologic macule, which is (by definition) flat but may occur in either the lepromatous or the tuberculoid form of leprosy, and an immunologic "macule," which may be either a (flat) macule or an elevated plaque but occurs only in the tuberculoid form of leprosy The lepromatous macule, for reasons which will be discussed presently, occurs relatively infrequently This fact has led to the practice of using the unqualified word "macule" almost entirely as a designation for the circumscribed, anesthetic, paucibacillary macules and plaques—the leprides of Unna which characterize the maculoanesthetic or "neural" or, as the Fifth International Congress for Leprosy named it, the tuberculoid form of the disease

LEPROMATOUS MACULES VERSUS "MACULES"

As Hansen observed over fifty years ago,[2] the "two forms [of leprosy] are clinically pretty sharply distinguishable" This state-

From the Clinic

Read at the Sixty-Eighth Annual Meeting of the American Dermatological Association, Inc, San Diego, Calif, April 26, 1948

1 Quotation marks will be used throughout this article wherever the word is being used in this sense rather than in the literal dermatologic sense

2 Hansen, G A, and Looft, C Leprosy in Its Clinical and Pathological Aspects translated by N Walker, Bristol, J Wright & Co, 1895

loss of hypersensitivity, with resultant reversal of the lepromin reaction to negative and transformation of the lesions from tuberculoid to lepromatous, may occur, though it is so infrequent that some workers have never observed it and some, indeed, doubt that it occurs I have seen it occur twice, both times in patients with large and numerous "major tuberculoid" lesions The first alarming sign was the tendency of both patients to have frequent exacerbations of the cutaneous lesions (tuberculoid reactions) Wade [22] described this process in detail in a few cases The reverse of this phenomenon of transition (i e, a change from the lepromatous to the tuberculoid type) seems to be much rarer, presumably because the patient will usually develop hypersensitivity and resistance to the bacillus early in the course of his infection if he is capable of developing them at all The only definite evidence that transformation in this direction can occur, in fact, was presented recently by Lauro de Souza Lima [23]

TUBERCULOID "MACULES" VERSUS LEPROMAS

In considering tuberculoid "macules" in contrast with lepromas, one is dealing with the easily distinguished "polar" lesions of the disease the two extremes, one representing victory for the patient's defensive processes and the other representing victory for Myco leprae All that was said about the differentiation of the lepromatous macule from the simple or anesthetic macule may be applied here The tuberculoid "macule" (whether macule or plaque) is regularly anesthetic, the leproma is anesthetic only if (as occasionally happens) it occurs in an anesthetic area of skin The tuberculoid "macule" typically contains few or no bacilli, even in reactions, it rarely contains the abundance of bacilli found regularly in a leproma The tuberculoid "macule" characteristically shows noncaseating, epithelioid cell tubercles, with abundant lymphocytes, histologically, the leproma has the architecture and composition of a fatty foreign body granuloma, or xanthoma, in which the lipid material is presumably furnished by the masses of Myco leprae, and in which lymphocytes are few

Clinical features, as with the flat macules, are less trustworthy, however, like flat tuberculoid macules, tuberculoid plaques are somewhat more likely to be solitary, or few, and asymmetric, and lepromas, generalized and symmetrically distributed Lepromas tend to develop earliest and most conspicuously on acral parts ears, forehead chin, buttocks, elbows and fingers Tuberculoid lesions show little or no

22 Wade, H W, and Rodriguez, J N Borderline Tuberculoid Leprosy, Internat J Leprosy 8:307 (July-Sept) 1940

23 Lima, L de S, and de Souza Campos, N Immuno-Biologic Anomalies in Leprosy Internat J Leprosy 16:9 (Jan-March) 1948

age, in darker skins the sweating tests described by Muir [7] and Degotte [8] (using intradermally administered pilocarpine or exercise) or by Myerson [9] and his associates (using methacholine), which seem to be just as sensitive may be used to better advantage [10] The important thing is the demonstration of nerve damage which is coextensive with the visible macule, this is highly characteristic of the maculoanesthetic—the "neural" or tuberculoid—form of leprosy

Clinical Aspects The remaining clinical features by which one may judge the hypothetic macule constitute much less useful criteria of its type The classic lepromatous macule tends to be multiple, and the tuberculoid, solitary, but many exceptions occur The lepromatous macule generally has a poorly defined border, often with fine pseudopod-like irregularities, the tuberculoid macule is usually sharply outlined By the same token, lepromatous macules tend to confluence and tuberculoid ones to discreteness Lepromatous macules are likely to occur on the trunk, a macule on the face or extremities is more commonly of the tuberculoid variety The lepromatous macule usually persists for many months or alternatively progresses into the clinical lesion known as a leproma, the anesthetic macule is likely to show evidence of regression within six months to a year None of these findings, however, is conclusive, and if the bacterioscopic and neurologic criteria are inconsistent one must resort to biopsy Indeed, biopsy should be done anyway, as a routine precaution

Histologic Changes Histologic changes in such early and minimally advanced lesions as the macules being discussed are pretty likely to be banal so far as the general pathologist's interpretation of them is concerned Ermakova, of Moscow,[11] found them so in a considerable series of anesthetic flat "macules" Wade,[12] on the other hand, found changes which he regarded as "nearly always in some degree tubercu-

7 Rogers, L, and Muir, E Leprosy, ed 3, Baltimore, Williams & Wilkins Company, 1946

8 Degotte, J Practical Application of Sweating Dysfunction to the Diagnosis of Leprosy, Rec tr sc med Congo, January 1942, p 135

9 Myerson, A, Loman, J, and Rinkel, M Human Autonomic Pharmacology VI General and Local Sweating Produced by Acetyl-Beta-Methyl Choline Chloride (Mecholyl), Am J M Sc **194** 75 (July) 1937 Arnold, H L, Jr The Sweat Response to Intradermally Injected Mecholyl Preliminary Report of Its Possible Use in the Diagnosis of Leprosy, Proc Staff Meet Clin, Honolulu **11** 75 (Aug) 1945

10 Arnold, H L, Jr The Intradermal Mecholyl Test for Anidrosis, A Diagnostic Aid in Leprosy, Internat J Leprosy **16** 335 (July-Sept) 1948

11 Ermakova, N The Histopathology of Simple Leprids, Internat J Leprosy **7** 495 (Oct-Dec) 1939

12 Wade, H W, and Rodriguez, J N The Skin Lesions of Early Leprosy II Observations in Cebu, Internat J Leprosy **5** 1 (Jan-March) 1937

Such hypersensitivity, once developed, usually results in eventual spontaneous cure of the infection, it may, however, be lost, with resultant transition of the case from the tuberculoid to the lepromatous category

The lepromin test appears to be a fairly trustworthy method of measuring this hypersensitivity, both in normal skin and in macules

The Clinic, South Hotel Street at Thomas Square (13)

ABSTRACT OF DISCUSSION

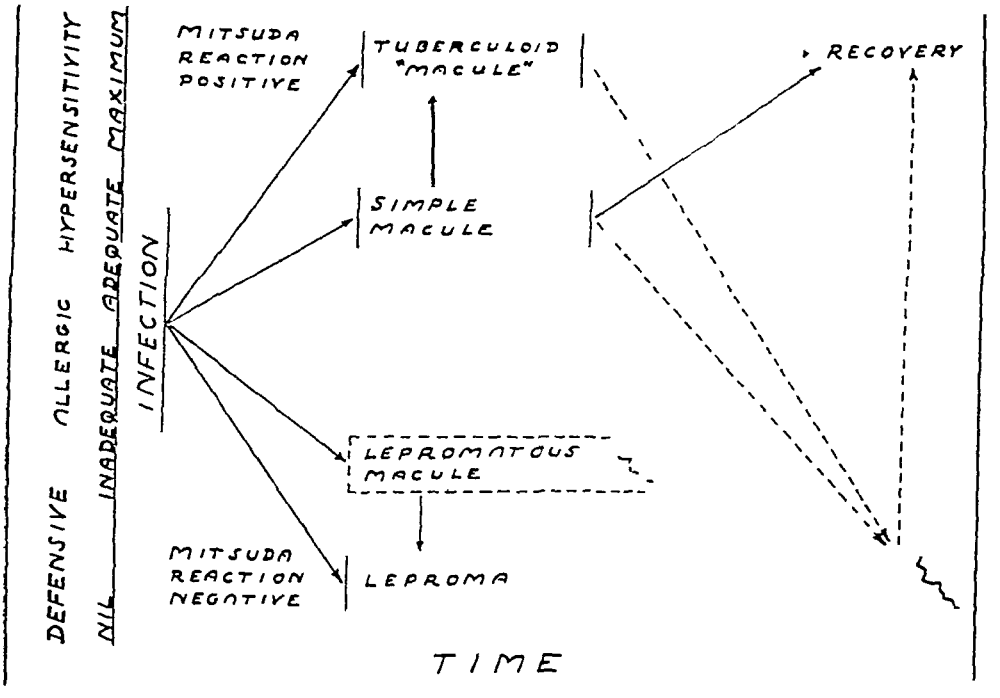
DR BRAULIO SÁENZ, Habana, Cuba The last time our Association met on the Pacific coast was in 1938, at Del Monte, Calif At that meeting I presented a paper on tuberculoid leprosy (ARCH DERMAT & SYPH **39** 456 [March] 1939), the first on this subject in North America The paper was written prior to the holding in Cairo of the Fourth International Congress for Leprosy and was read shortly thereafter It was at that congress that the South American classification of leprosy was rejected and the Cairo classification adopted

My paper, being a pioneer one and based on a limited number of observations, was no doubt incomplete and not devoid of some minor erroneous interpretations Ten years later, on April 10, 1948, the Fifth International Congress for Leprosy took place in Habana, and the South American classification (now known as the classification of Habana) was adopted Dr Arnold has very aptly outlined his paper on this classification, which, for the time being, is the only one tenable, because it is based on the following points (1) the morphology, or clinical aspect of the lesions, (2) immunologic reactions, (3) bacteriologic criteria and (4) a more or less definite histopathologic picture

The presenter stresses the importance of these fundamental bases and discusses the position of the indeterminate groups, previously called uncharacteristic This, as he indicates, may be the possible weak point of this classification, but one must remember that, not only in leprosy, but also in many other dermatologic processes, only the evolution determines the real position of certain cases and that borderline cases are often observed In addition, this group, in the majority of cases, presents a negative reaction to the Mitsuda test, which is a possible indication of future transition to the lepromatous form

The publications of F Fischl (*Dermat Ztschr* **55** 274 [March] 1929), and of Jadassohn (ARCH DERMAT & SYPH **21** 355 [March] 1930) and the communications of J Darier, Civatte, P Woringer and H Gougerot to the International Dermatological Congress at Budapest in 1935 (Deliberationes Dermatologorum Internationalis, IX-1, Budapest, September 1935, Leipzig, Johann Ambrosius Barth, 1936) made important contributions explaining the role of the biologic reactions of immunity on the morphologic aspects of the cutaneous lesions, nevertheless, some points remain unanswered For example, some have denied the possibility of the transformation of the tuberculoid lesions to the lepromatous form, despite such denial, this transformation is an established fact Dr Arnold has observed 3 such cases, and I have seen 4 Some three months ago, I requested Dr Nelson Souza Campos who has had considerable experience in the treatment of patients in the Sanatorio Padre Bento São Paulo, Brazil, for his opinion on the subject He replied to the effect that he had observed 64 cases of tuberculoid leprosy of the reactional type which had undergone transformation to the lepromatous type All cases were observed in patients in leprosy asylums The possible explanation is that these patients had been superinfected from other lepromatous patients This explanation did not apply to my patients who were all encountered in my private

presumably uninfected persons, it regularly produced little or no reaction in the great majority of patients with the "tubercular" (*the nodular*, or lepromatous) form He extended and amplified his observations in a series of reports, which received little attention in this country until the publication of a paper by his student, Hayashi, in 1933 [15] His observations have since been widely confirmed Numerous studies have been made in an effort to improve and standardize the test by purification and fractionation of the test material These have not been especially rewarding, however, since the crude preparation seems as potent as and no less specific than, its various fractions [16]



Diagrammatic oversimplification of the major cutaneous lesions of leprosy as functions of (1) "defensive allergic hypersensitivity" to the bacillus and (2) time Note that this hypersensitivity may already exist at the time of infection, that it may either increase or decrease after infection occurs, that it may be demonstrated by a positive Mitsuda reaction, that it results, in general, in self limited lesions known as "macules," that its failure to develop results in essentially persistent or progressive lesions and that it rarely, if ever, develops late in the course of the disease Note, too, that exceptionally this hypersensitivity may be lost, resulting in transition of the disease to the lepromatous form and that, also exceptionally, recovery will occur in a lepromatous case, without, however (or sometimes with?), transition through a tuberculoid phase

The term "defensive allergic hypersensitivity" is to be taken loosely, not literally And the prognosis as indicated does not take into account the effect of treatment with sulfone derivatives

15 Hayashi [14b]

16 Davey, T F Some Observations on the Role of Allergy in Leprosy, Leprosy Rev **17** 42 (July), 75 (Oct) 1946

this "transitional" variety, they may merely be cases undergoing a single transitory tuberculoid reaction In reply to Dr Montgomery's query regarding sarcoid I was not aware that the lepromin test was necessarily negative in sarcoid, or at least in sarcoid not due to leprosy It had been my feeling that in areas where leprosy was not endemic, positive reactions to lepromin would be relatively unusual and that many cases of sarcoid would therefore, in such areas, be fairly likely to have negative Mitsuda reactions—permitting tuberculoid leprosy to be excluded with fair accuracy This situation does not exist in Hawaii, or in any place where leprosy is endemic However, if anergy in sarcoid is expressed in a negative reaction to lepromin as well as in a negative reaction to tuberculin, the problem is greatly simplified In answer to Dr Weidman, I believe that *Nachtblau* cannot be purchased at the present time, but Dr Reenstierna has promised to give me a small quantity of it, and perhaps some more can be obtained through him at the University of Uppsala in Sweden As to the Fite technic, Fite himself has virtually abandoned it in favor of the Feraca procedure, which is certainly far simpler and more rapid and which he believes is equally satisfactory for finding rare organisms My colleague Dr Tilden and I still prefer to see blue-black bacilli against a pale orange-yellow background

well defined, noncaseating, epithelioid cell tubercles and no or comparatively few bacilli; bear out this statement, in accordance with the observations of Jadassohn and Lewandowsky It seems probable that in these lesions there is elaboration of abundant antibody by the histiocytes in the skin, and a resultant antigen-antibody reaction which effectively eliminates the bacilli Why this inflammatory reaction is rarely accompanied with necrosis when it occurs in the skin, and is usually accompanied with it when it occurs in the nerves, is not clear, but this finding has often been reported,[20] and my observations in Hawaii have regularly confirmed it Of course this necrosis of nerve tissue is the reason for the regular occurrence of anesthesia or anhidrosis in even the earliest "macules," and it has led to the confusion begun by Danielssen and Boeck [21] (and checked only for a time by Hansen and Looft [2]), resulting from the designation "anesthetic" or "nerve" or "neural" for cases of this form of the disease and also for lepromatous cases with more nerve damage than cutaneous damage

It may be significant that there is not necessarily any difference between this tuberculoid response, produced by presumably living Myco leprae, and a positive Mitsuda reaction, produced by dead ones, for, indeed, as Davey [16] pointed out, if the former happens to be vigorous and intense enough, or to be accompanied by sufficiently pronounced fixation of the bacilli in the tissues, it may run the same swift and benign course as the Mitsuda test, with final complete resolution in a few weeks or months Ordinarily, however, the multiplication of bacilli, ahead of (or in) the advancing border of the lesion, is able to keep slightly ahead of the development of the defensive tissue reaction, so that gradual spread occurs, and only after some months, or even longer, does either the "anchoring" of the bacilli or the more effective production of antibodies permit all the organisms to be destroyed, so that the lesion heals Healing often occurs in the central zone and spreads peripherally, so that annular lesions from a few millimeters to several decimeters in diameter are formed, and "cockade" patterns, produced by successive fluctuations in the vigor of the antigen-antibody reaction, are not unusual Such patterns are not infrequently observed in patients whose disease is undergoing transition from the tuberculoid to the lepromatous type

The effectiveness and persistence of this combined defensiveness and hypersensitivity may vary widely Transitory relapses after complete or partial healing of the lesions are not rare Even gradual, persistent

20 Ota and Sato [18] Pardo-Castello, V , Tiant, F R , and Piñeyro, R Nerve Lesions of Leprosy, Arch Dermat & Syph *55 783* (June) *1947*

21 Danielssen, D C, and Boeck, C W Traite de la spedalskhed ou elephantiasis des grecs, Paris, J -B Baillière, 1848

true Nevertheless, the possibility led Niles[6] to attempt cure of the condition by extirpation of the central spots in the hope of interrupting the assumed attraction of pigment thereto Niles reported failure to influence the depigmenting process by this means Nor did the central pigmentations tend to recur, as one would expect they possibly would if the theory of centripetal drainage of pigment had any virture Moreover, in undisturbed cases, the central nevi or hyperpigmentations according to this theory, should grow larger for as long at least as the process is active This situation we believe and will show does not exist

Leider and Cohen,[3] among many others before them,[7] maintained that leukoderma acquisitum centrifugum is nothing more than banal vitiligo that starts accidentally, or for the particular but unknown reason that causes all depigmentation, around preexisting moles Kuske,[4c] who was previously quoted, expressed disagreement in the following words " Sharply delimited, round or oval, depigmented spots without a visible nevus can readily be confused with true vitiligo At present it appears to me that a distinction [between Sutton's phenomenon and vitiligo] is justifiedly made "[8] Kuske based his conviction on a table of clinical differences which we do not find persuasive

In support of the contention that leukoderma acquisitum centrifugum is merely a variant of simple vitiligo, we report by photographs the following instances of spontaneous disappearance of the central maculopapules while the patients were under prolonged observation We never saw nevi come into being, nor could the patients assert that the nevi had not been present long before the depigmentation had begun We noted established vitiliginous areas increase in size both centrifugally and centripetally, i e , away from and into the hyperpigmented centers and we saw new depigmentations begin around other old nevi The nevi seemed to be invaded by the depigmenting process and were gradually blotted out We can make nothing more of this phenomenon than the usual progression of vitiligo The central hyperpigmented areas persist only so long as it takes the depigmenting mechanism, whatever it may be, to bleach them completely The reason that it takes as long as it

6 Niles, H D Leukoderma Acquisitum Centrifugum, Arch Dermat & Syph **43** 357 (Feb) 1941

7 (*a*) Sutton[1] (*b*) Hyde[2] (*c*) Hebra F and Kaposi, M On Diseases of the Skin Including the Exanthemata, translated and edited by W Tay, London The New Sydenham Society, 1874 vol 3 p 180 (*d*) Stokes, J H Leukoderma Acquisitum Centrifugum (Sutton), Arch Dermat & Syph **7** 611 (May) 1923

8 The original read " Scharf begrenzte, runde oder ovale depigmentierte Herde ohne sichtbaren Naevus konnten leicht mit echter Vitiligo verwechselt werden Zur Zeit scheint mir die Trennung gerechtfertigt

real predilection for these parts A sharply defined and elevated border or a clearing center is much more likely to be manifested in a tuberculoid lesion than in a leproma, though the sharply clear center, with a less clearly defined outer margin, suggests the leproma rather than the tuberculoid lesion Norman Sloan [24] pointed out that lepromas have a strong tendency to respect facial and other natural grooves and creases, such as the nasolabial fold and the angle between the root of the nose and the inner corners of the eyes, a tuberculoid plaque will often invade and involve such areas Involvement of the mucous membrane (of the eye, mouth, nose, throat and larynx) and testicular involvement occur only in lepromatous cases Nerve involvement occurs regularly in both lepromatous and tuberculoid cases, but nerve damage is produced only slowly by the gentle, passive, bacteriophagic lepromatous response, whereas it is produced early and rapidly by the vigorous, defensive, bacteriolytic tuberculoid response

SUMMARY AND CONCLUSIONS

The flat macules and elevated "macules" of leprosy apparently represent circumscribed cutaneous areas of acquired allergic hypersensitivity to the nucleoprotein of Myco leprae

If this hypersensitivity is lacking or inadequate to destroy the organisms, the macule is called a lepromatous macule, and it can usually be identified as such by the abundance of bacilli in it and its failure to manifest anesthesia or other evidence of nerve damage

If this hypersensitivity is adequate to destroy the organisms, the lesion is then often spoken of simply as a "macule" (or, better, a tuberculoid plaque), and it can usually be recognized by its relative lack of bacilli and the regular occurrence of evidence of nerve damage throughout its visible extent If such lesions are flat they are sometimes called "simple macules" or "anesthetic macules", if they are elevated they are usually called "tuberculoid macules" Both terms were included under Unna's word "leprides"

The development of an adequate degree of resistance and allergic hypersensitivity to Myco leprae results in the establishment of a relatively favorable form of leprosy which has been known as the "anesthetic" (Danielssen, 1847), "maculoanesthetic" (Hansen, 1895), "neural" and, more recently, "tuberculoid" form

The failure of development of such a state following infection with Myco leprae results in the establishment of an unfavorable form of leprosy known as the "tubercular" (Danielssen), "nodular" (Hansen), "cutaneous" and, more recently, "lepromatous" form

24 Sloan N R Personal communication to the author

marked to have had a preexisting nevus at one time, but from which a biopsy specimen was taken after spontaneous depigmentation had occurred, showed absence of nevus cells and only the negative picture of vitiligo When the central spot is an indisputable nevus rather than an ephelis or lentigo, another nice question is that of what becomes of the nevus cells on disappearance of the mole Are they destroyed or are they dispersed? However that may be, we think that any person with as many lesions as these, some adorned with and some bare of

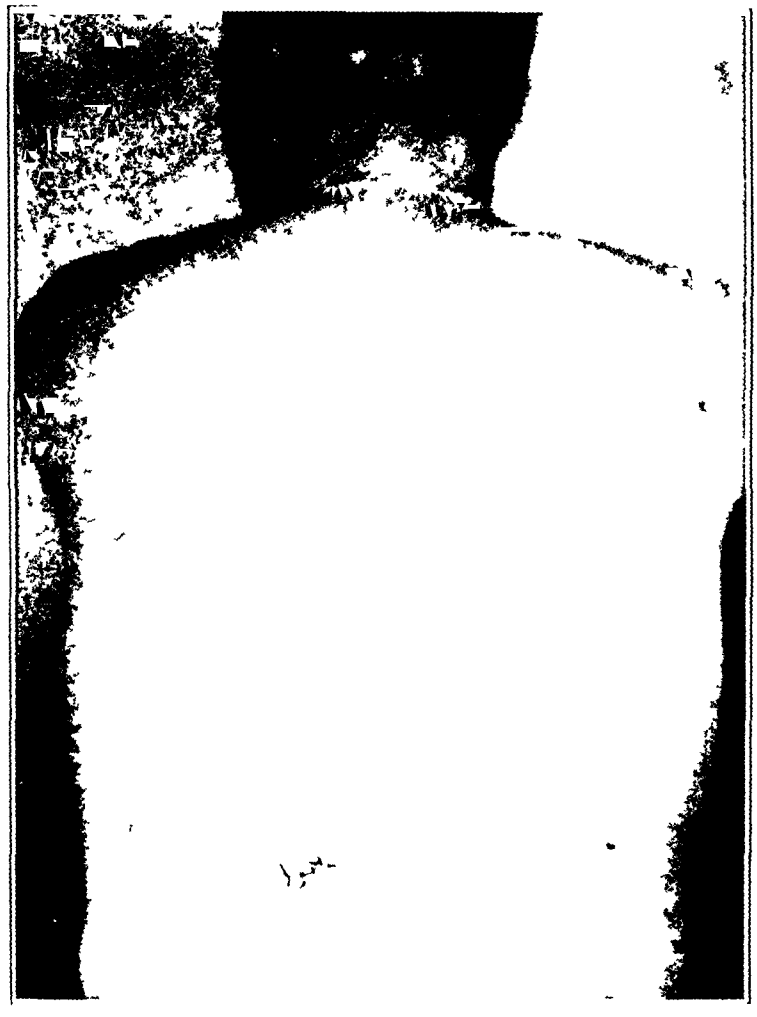


Fig 2—Leukoderma acquisitum centrifugum Compare with figure 1

the central spot, may be assumed to have had more central pigmented maculopapules to begin with, some of which had disappeared by the time the first examination was made This must have been the situation for the patient in case 1 of Leider and Cohen (fig 2) whose photograph shows a nearly identical picture

Figures 3 and 4 are "before" and after photographs of the patient in case 2 in the article of Leider and Cohen The spontaneous dissolution of the central preexisting nevus was complete What appears in the picture as a pigmented center was erythema, which photographed

practice Therefore, I should like to ask Dr Arnold whether his cases were encountered in an asylum or in private practice Through the action of the sulfone drugs, the reverse of this transformation was reported to the Fifth International Congress for Leprosy by Lauro de Souza Lima (*Internat J Leprosy* **16** 127 [April-June] 1948) Lepromatous leprosy was transformed into the tuberculoid type The histopathologic changes from one form to the other were checked at different dates, the tissular changes appearing first as the expression of an acquired immunity, later the reaction to the Mitsuda test became positive, and as a final stage came the curability of some of the cases Before closing I wish to congratulate Dr Arnold heartily on his timely paper, it is simple and concise, and it gives complete descriptions of the polar and of the indeterminate forms of leprosy, as well as valuable information to the dermatologist respecting correct diagnosis, prognosis and epidemiology of the disease

I also wish to express my satisfaction for the opportunity I have been given to open the discussion on this excellent contribution, in addition, it gives me pleasure to inform Dr Arnold that I have been requested to advise him that he has been proposed as a correspondent member of Sociedad Cubana de Dermatologia y Sifilografia, and of Academia Espanola de Dermatologia y Sifilografia, as a reward for his qualifications as a dermatoleprologist

DR LOUIS WINER, Los Angeles I wish to compliment Dr Arnold on his excellent paper My associates and I have had such cases on two occasions in Los Angeles These cases histologically were definitely tuberculoid in structure On use of the Ziehl-Neelsen stain, numerous acid-fast bacilli were observed The reaction to the lepromin test was negative Because of these observations we were unable to classify the patients However, the indeterminate group provides a classification modification, so that now these patients can be classified I think that the histologic characteristics of tuberculoid formation are indicative that a better prognosis can be expected than if these characteristics were not present

DR HAMILTON MONTGOMERY, Rochester, Minn I should like to ask Dr Arnold and Dr Saenz about recent reports in the literature regarding the reaction to lepromin in patients with sarcoid and tuberculosis It would appear that in sarcoidosis there is a negative reaction, whereas in active pulmonary tuberculosis the reaction may be positive If such observations are substantiated, the lepromin test might be of diagnostic value in northern climates where leprosy is not endemic in distinguishing between an annular sarcoid and a tuberculoid leprosy Both show an epithelioid tuberculoid reaction histologically, so that in older literature in Scandinavian countries the question was raised as to whether the patient had sarcoid or tuberculoid leprosy Tuberculoid leprosy, I understand, gives a positive lepromin or Mitsuda reaction

DR FRED D WEIDMAN, Philadelphia I should like to ask Dr Arnold whether he is able to get a supply of *Nachtblau,* which Dr Pardo-Castello told us about and which is superior to the ordinary Ziehl-Neelsen technic for staining the bacilli

I have tried to secure a supply, without success Does he think that the Fite technic is also superior?

DR HARRY L ARNOLD JR, Honolulu, Hawaii I am obliged to all the discussers Dr Saenz asked whether the transitional cases were private or asylum cases they were all asylum cases, 1 in Mexico and 2 in Hawaii, and all showed typically tuberculoid annules with the "cockade" pattern, with numerous bacilli and (in those seen in Hawaii, at least) a negative reaction to the lepromin test Dr Winer's cases with tuberculoid lesions with numerous bacilli may be examples of

being during life they tend to be permanent They may, relatively rarely, disappear as a result of trauma or other uncertain reasons In leukoderma acquisitum centrifugum they seem to be invaded by the same depigmenting process that concurrently affects the ordinary skin

F Parkes Weber [10] speculatively suggested that there may be a constant law embracing the phenomenon of depigmentation of this sort,

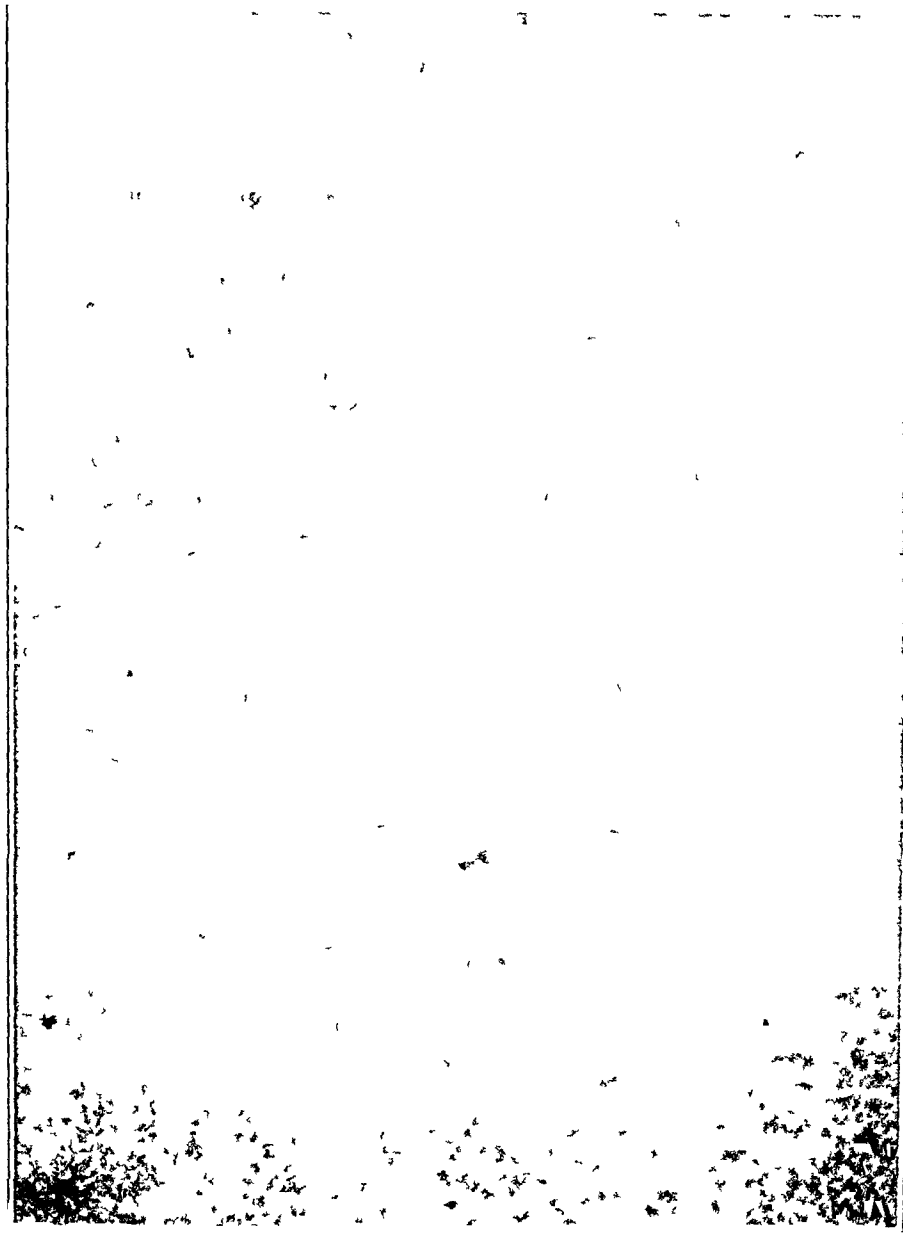


Fig 4—Same case as in figure 3, about eighteen months later The darker portion in the center is erythema, not pigment

as follows Nevi predispose to circumferential depigmentation in an amount that is in direct proportion to their size Stokes [7d] noted, and we have too that leukoderma acquisitum centrifugum is rather common

10 Weber F P A Law Regarding the Distribution of Pigmented (Leucodermic) Patches of Vitiligo, When They Are Superadded to Mole-Like Nevi Brit J Child Dis **21** 202, 1924

FATE OF CENTRAL NEVUS IN LEUKODERMA ACQUISITUM CENTRIFUGUM

MORRIS LEIDER, M D
BROOKLYN
AND
ALEXANDER A FISHER, M D
WOODSIDE, N Y

MOST accounts of leukoderma acquisitum centrifugum do not make clear what, if anything, ultimately happens to the central hyperpigmented spots that make this condition so distinctive Neither Sutton,[1] who originally described the picture minutely after Hyde[2] had noted it, nor Leider and Cohen[3] in their recent review discussed the eventual disposition of the moles However, a few of the intervening observers,[4] particularly in the foreign literature, remarked that the central pigmentations sometimes disappear To quote one, Kuske[4c] wrote that " one gets the impression, from history and objective finding, that in some of the lesions undergoing enlargement, the nevus in the center is gradually obliterated by the depigmenting process "[5]

In 1 of Sutton's 2 original cases, the mother of the patient (a child), stated that the central spot had not been present before the onset of the depigmentation In consequence of such observations on the part of patients or their close relatives, some authors have theorized that the pigmented areas in the centers form because melanin, or propigment, drains from the periphery into a centripetal concentration We doubt that these observations are correct and that the resultant theory is

1 Sutton, R L An Unusual Variety of Vitiligo (Leukoderma Acquisitum Centrifugum) Report of Two Cases, J Cutan Dis **34** 797, 1916

2 Hyde, J N Vitiligo with a Central Mole, J Cutan Dis **24** 54, 1906

3 Leider, M, and Cohen, T M Leukoderma Acquisitum Centrifugum, Arch Dermat & Syph **57** 380 (March) 1948

4 (*a*) Gougerot, H, and Carteaud, A Maladie de Sutton avec régression d'un naevus pigmentaire pendent l'accroissement de l'achromie, Bull Soc franç de dermat et syph **41** 1526, 1934 (*b*) Meirowsky, E Leukoderma Acquisitum Centrifugum (Sutton), in Jadassohn, J Handbuch der Haut- und Geschlechtskrankheiten Berlin, Julius Springer, 1933, vol 4, pt 2, p 1000 (*c*) Kuske, H Ueber Leukoderma acquisitum centrifugum (Sutton), Dermatologica **88** 282, 1943

5 The original read " bekommt man durch die Anamnese und durch den objectiven Befund den Eindruck dass bei einigen sich ausdehnenden Elementen auch der Naevus im Zentrum allmahlich dem Depigmentierungsprozess verfallt "

IS LICHEN URTICATUS A FORM OF URTICARIA?

THEODORE CORNBLEET, M D
CHICAGO

SINCE the time of Bateman, who accurately described lichen urticatus, there has been controversy about the nature and pathogenesis of this disorder In successive periods of dermatologic history new ideas have developed about this disease, reflecting the thoughts and subject matters current at the moment Thus, at one period, foods and bowel disturbances were said to be causative, in harmony with the emphasis placed on intestinal putrefactions and toxemias At present lichen urticatus is mostly thought of as a form of urticaria, in keeping with the keen awareness of the phenomena of allergy, and is so classified in the textbooks

There has been so much written on lichen urticatus that there would seem to be little excuse for still further overtaxing what has been for the most part theoretic discussion Only new evidence can be an adequate reason for reopening the subject The recent development and use of the antihistaminic or antiallergic synthetic drugs may permit one to survey the problem from a fresh perspective Toward that end the following several case histories are presented

CASE HISTORIES

1 T K R, a Negro girl 4 years old, had a papular eruption mostly on the extensors of the extremities and a few lesions on the trunk and the face, which was diagnosed as lichen urticatus The mother said it was present the previous two summers, too After three weeks' use of diphenhydramine hydrochloride (elixir benadryl hydrochloride®) there was no improvement in the appearance of the lesions or apparently in the distress caused by the itching There was marked betterment after three more weeks during which she was treated simultaneously with parathyroid injection U S P and calcium lactate

2 Z P, a boy 5 years old, had an eruption which had been present in the same form the previous year It was thought to be lichen urticatus Four weeks' use of diphenhydramine hydrochloride failed to produce any evident improvement in the lesions, even though the child slept better and was more restful

3 J O M, a woman 23 years old, had a pruritic papular eruption on the extensors of the arms and legs and scattered elements on the trunk Some of the lesions were acuminate and there was severe pruritus There was no grouping, nevertheless, she was given a course of sulfapyridine treatment on the pos-

From the Department of Dermatology University of Illinois College of Medicine, Service of Dr F E Senear

does for the central pigmentation to disappear is perhaps that the amount of pigment is so excessive or that nevi resist withering on account of their inherent good capacity to produce pigment Also, it seems to us that the very disappearance of the central pigment in this manner disposes of theories like those of Feldman and Lashinsky[9] and others that leukoderma acquisitum centrifugum is a nevoid disease *sui generis* If one wishes to admit vitiligo as a nevoid anomaly (tardus), then leukoderma acquisitum centrifugum is a nevus, too, but still a variant of vitiligo

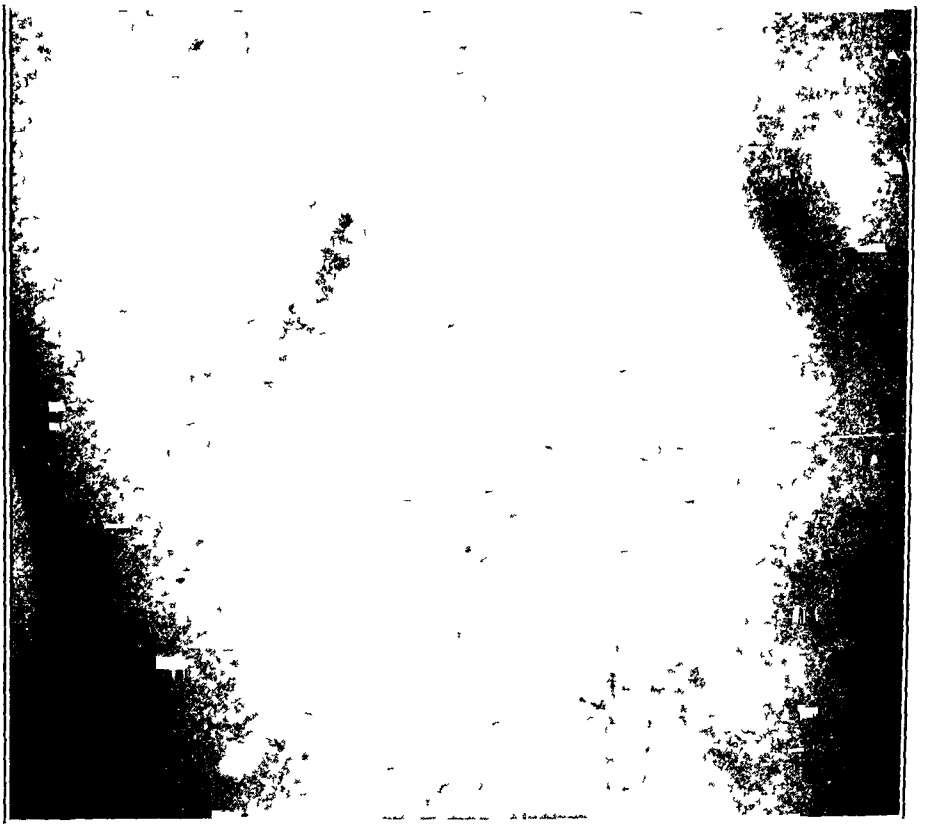


Fig 1.—Leukoderma acquisitum centrifugum, showing lesions with and without central pigmented spots What appears to be residual pigment in some instances is erythema

Figure 1 shows comparable circles of vitiligo, some bearing the central pigmented spots and some lacking them When the patient was first seen by one of us (A A F), almost all lesions bore a nevus Many of these nevi are known, from periodic examination at regular intervals over several years, to have vanished, leaving only the enlarging vitiliginous areas In this case, histologic examination of a site which was

9 Feldman S , and Lashinsky, I M Halo Nevus Leukoderma Centrifugum Acquisitum (Sutton) , Leucopigmentary Nevus, Arch Dermat & Syph **34** 590 (Oct) 1936

clusive toward allying this entity with urticaria They attest to the efficacy of parathyroid extract used in conjunction with calcium in the former, compared with the mediocre results in the latter

SUMMARY

The failure of the antihistaminic or antiallergic agents to influence lichen urticatus favorably is presented as further evidence to disprove any connection of this condition with urticaria

1819 West Polk Street

dark In the flesh it was red and it would show so on a color photograph The interim was eighteen months, and during this period the gradual progressive depigmentation had been noted on several occasions In both of these cases in which we were able to follow the extinction of the nevi, we saw that as the pigmentation faded it left erythema, which then eventually blanched and blended into the surrounding pallor of the vitiligo In addition, whether the original



Fig 3—Leukoderma centrifugum acquisitum, beginning

pigmented spot was a macule or a papule, the end result was always flat and level with the neighboring skin

It may be argued that the central hyperpigmentations in leukoderma acquisitum centrifugum first come into being because melanin drains to the center, thus forming the moles, and that they then get involved by the "vitiligizing" process which erases them We remember no report in which a medical observer claimed to have witnessed the first event of nevus formation Therefore, it appears much more likely to us that nevi, lentigines and ephelides, which are so common to all, preexist or arise in the ordinary mysterious manner Whenever they come into

group as "the anhidrotic type of hereditary ectodermal dysplasia," a term which we believe to be most descriptive, because it emphasizes both the cause and the most important clinical symptom of the syndrome, inability to sweat

According to recent reviews of the literature including those of Kaalund-Jørgensen and Christensen [6] and Helweg-Larsen and Ludvigsen,[7] approximately 80 cases of the complete anhidrotic syndrome had been reported prior to 1947 The syndrome has a wide racial distribution, reports having been made from many of the countries of North America, Europe and Asia

Although this triad of symptoms, namely, hypodontia, hypotrichosis and anhidrosis, has been observed many times during the past hundred years, the literature we have read includes no observation of universal anhidrosis that occurred alone This is unusual when one considers that universal aplasia of other single components of the skin, such as hair or pigment to produce alopecia totalis or albinism, respectively, is not infrequent

CLINICAL CHARACTERISTICS

The patients affected by the anhidrotic type of ectodermal dysplasia resemble each other to a remarkable degree because of their unusual facies, which is somewhat suggestive of congenital syphilis and is characterized by high, wide brows, prominent frontal bosses, depressed nasal root and bridge, thick lips with radiating furrows about the mouth, and satyr-like ears

The skin of these patients is unusually soft, thin and feminine Total or almost total lack of sweat gland function under all environmental conditions is the most important physiologic feature, sebaceous gland activity is usually diminished to a variable degree, but apocrine function may be normal The mammary glands may be normal or, as described by Clarke and McCance [8] as well as others, they may be deficient or absent

A delayed appearance and a marked deficiency of development of scalp hair eyebrows and eyelashes and lanugo are frequent, but there is often little uniformity in the degree of development of hair beginning at or after puberty, the beard being more frequently normal, while axillary and pubic hair is either scanty or absent Scalp hair is usually stiff fine and short

6 Kaalund-Jørgensen O and Christensen J T Congenital Ectodermal Dysplasia of the Anidrotic Type, Acta dermat-venereol **22** 1-23 (Feb) 1941

7 Helweg-Larsen, H T, and Ludvigsen, K Congenital Familial Anhidrosis and Neurolabyrinthitis, Acta dermat-venereol **26** 489-505 (May) 1946

8 Clarke R E, and McCance, R A Familial Sex-Linked Ectodermal Dysplasia with Incomplete Forms, Arch Dis Childhood **9** 39-44 (Feb) 1934

if sought for and that non-nevoid conditions, like the lesions of psoriasis, syphilis, Boeck's sarcoid and burns, are frequently surrounded by leukodermatous halos, and he therefore postulated that a common physicochemical inhibition of melanogenesis is at the basis of all such depigmentations It seems to us that hyperpigmentations too are common around many dermatoses, including those mentioned by Stokes, none of which is commonly associated with problems of melanogenesis Coupling our own observations with those of Weber and Stokes, we should say that there may be a law about pigmentary dyscrasia which may be formulated as follows Any abnormality of the skin, congenital or acquired, perceptible or imperceptible, may become a locus of pigmentary disturbance in directions of excessive formation and concentration or of inadequate formation and dispersion When the disturbance is in the direction of depigmentation, is imperceptible and is of point source and unknown cause on apparently normal skin, the clinical picture appears like that of banal vitiligo When the predisposing disturbance, again in the direction of depigmentation, is an obvious lesion, then the clinical lesion may be leukoderma acquisitum centrifugum, with either a nevus or some other non-nevoid condition in the center In the latter event, the word leukoderma is a most proper designation because the depigmentation is related to a known proximate cause In reverse, the very same types of pigmentary disturbances may in other cases eventuate in chloasma-like changes Indeed, vitiligo itself often seems to be accompanied with hyperpigmentation at its border, which observation supports a concept of melanogenesis as a mechanism of such delicate balance that the very same influence, or train of influences, seems to be able to direct it into the direction of either hypopigmentation or hyperpigmentation or of both simultaneously

820 Caton Avenue (18)

4514 Forty-Eighth Street

ducts There is usually a similar marked deficiency of pilosebaceous structures, but this anomaly is more variable in degree The epidermis is usually thinner than normal, and there is likewise a reduction in width of the cutis, but collagen and elastic fibers and blood vessels are normal in appearance Sunderman [11] reported normal apocrine glands but absent eccrine glands in his biopsy material from the axillas of 2 patients In the anhidrotic patients of Helweg-Larsen and Ludvigsen, as microscopic sections revealed, the number of sweat glands was much reduced, while the glands which were present were hypertrophic

Biopsies of the thin, dry mucous membranes of the mouth and upper respiratory passages have revealed hypoplastic changes in the epithelium as well as in the underlying glands, corresponding with the clinical appearance of these structures

PHYSIOLOGIC CHARACTERISTICS

It must be pointed out that evidence of complete anhidrosis based on single or multiple biopsies is incomplete, even though the sites include the palm or the sole and serial sections reveal no sweat glands Specific physiologic studies of temperature and sweat are necessary for proof of complete anhidrosis At ordinary environmental temperatures and at rest, when the sweat glands are not needed to dissipate heat, the amount of insensible perspiration given off by cutaneous transudation of water is quite sufficient to maintain a normal temperature of the body in anhidrotic as well as in normal patients However, at high environmental temperatures, when a temperature of 98 6 F can be maintained in a normal person by the function of sweat glands, the temperature of the anhidrotic patient rises rapidly to extremes of 102 to 104 F , and the pulse and respiratory rates increase proportionately in a vain attempt to dissipate heat

Although the amount of perspiration of anhidrotic patients is inadequate to maintain a normal body temperature at high environmental temperatures, Felsher [12] has observed that some few sweat glands may be present and functioning in these patients By applying a starch-iodine mixture to the skin of his patients, he saw a few small areas where sweat was being produced when the skin was exposed to heat He therefore suggested that the term "hypohidrosis" rather than "anhidrosis be applied to this group of patients

11 Sunderman, F W Persons Lacking Sweat Glands Hereditary Ectodermal Dysplasia of the Anhidrotic Type, Arch Int Med **67** 846-854 (April) 1941

12 Felsher, Z Hereditary Ectodermal Dysplasia Report of a Case with Experimental Study, Arch Dermat & Syph **49** 410-414 (June) 1944

sibility that the eruption was dermatitis herpetiformis There was no good effect from this therapy She was then given 300 mg of tripelennamine hydrochloride (pyribenzamine hydrochloride®) daily for ten days without visible or subjective improvement Itching largely subsided and much of the eruption was gone after a month of the use of parathyroid injection U S P and calcium lactate

4 D A, a white boy 8 years old, had a papular eruption mostly on the extensor surfaces of the extremities A few lesions had puffy bases, and a frank wheal was present at one site There was itching He was thought to have lichen urticatus The lesions remained largely unchanged after two weeks' use of diphenhydramine hydrochloride

5 C N, a Negro girl 6 years old, had an itching eruption which was believed to be lichen urticatus Three weeks' use of diphenhydramine hydrochloride effected no apparent improvement in her cutaneous condition

COMMENT

The greatest success attending the use of the antihistaminics has been in connection with urticaria It is reasonable to assume that if lichen urticatus is a form of urticaria peculiar to children it should react somewhat similarly to therapeutic agents which benefit patients with urticaria This small series of patients derived no benefit from the newer antiallergic agents in contrast with the happier results commonly seen in ordinary urticaria This raises again doubts that lichen urticatus is primarily an urticarial process Pruritus is common to both, but is present, too, where there is no suspicion of urticaria The mere presence of wheals as one of the primary lesions should not be binding to a diagnosis of urticaria It would seem tenuous to make their presence in urticaria pigmentosa a proper cause for including the latter among the urticarias even though its origin remains unknown Wheals may at times be found in diverse entities, even as the initiating event of a folliculitis or a furuncle

Walzer and Grolnick,[1] in an intensive study of lichen urticatus, employing modern methods of dealing with allergy, were unable to relate this disease to such a process Pillsbury and Sternberg [2] said

> the theory that the nature of this disease is allergic has been commonly held, and most investigations have been concerned in the attempt to prove or disprove this contention We believe that the evidence supporting such a view is extremely meager and that further study along the lines of allergy, unless some unique approach is devised, will probably be fruitless

They reviewed the studies of various authors whose work had failed to resolve the beclouded pathogenesis of lichen urticatus and been incon-

1 Walzer, A, and Grolnick, M Relation of Papular Urticaria and Prurigo Mitis to Allergy, J Allergy **5** 240, 1934

2 Pillsbury, D M, and Sternberg, T H Lichen Urticatus (Papular Urticaria) Treatment with Parathyroid Extract, Theoretical Consideration of Etiology, Am J Dis Child **53** 1209 (May) 1937

between the second and third months of gestation, first in the region of the eyebrows and forehead Between the fourth and fifth months, rudiments of hair begin to grow from these follicles 2 The earliest evidence of nails appears during the third month, but formation of the nail matrix occurs later, at the fifth month of gestation 3 Sebaceous glands originate as lateral outgrowths of the hair follicles during the fifth month 4 Sweat gland anlages appear first on the tips of the phalanges between the fourth and fifth months, and on the proximal portion of the extremities and the trunk by the end of the sixth month, development of these glands is almost complete before birth

The remainder of the embryologic data concerned in the syndrome is as follows 1 The teeth have a double origin, the enamel organ develops from the ectoderm, and the dentine, pulp and cement develop from the mesoderm By the seventh week of gestation, the dental lamina of the ectoderm shows circumscribed thickenings where the future teeth are to be formed At eight weeks, the underlying mesodermal cells begin their growth and differentiation to form the future mesodermal portion of the teeth 2 The milk ridge appears in the embryo between the fifth and sixth weeks of intrauterine life, and from it, in the pectoral region, papilla-like anlages of the mammary glands develop early in the fifth month 3 The neural tube, from which the entire nervous system, the adrenal medulla and a portion of the pituitary gland develop, is completely closed and separated from the overlying epidermis by the beginning of the second month of gestation

Since few reports of definite abnormalities of the nervous system in anhidrotic patients have been recorded, it seems probable that the pathologic process resulting from the defective gene or genes begins to affect the development of the epidermal structures during the second fetal month However, the lens, although undergoing separation from the ectoderm during this time, enjoys, to our knowledge, complete immunity Although the mechanism of genetic transmission of these defects is fairly well understood, at this time the method by which certain structures appear to be haphazardly affected by these genes is not at all clear

Most observers have agreed that the pathologic process is probably an aplasia and not an atrophy because degenerative changes in ectodermal structures rarely have been seen in tissue sections, the structures instead appear never to have begun or just barely to have begun to differentiate

DIFFERENTIAL DIAGNOSIS

There are four diseases which usually have enough symptoms in common with the anhidrotic syndrome to be considered in its differential diagnosis The accompanying table is a brief summary of their essential similarities and differences

HEREDITARY ANHIDROTIC ECTODERMAL DYSPLASIA

A Clinical and Pathologic Study

BETTE Y UPSHAW, M D
Fellow in Dermatology and Syphilology, Mayo Foundation
AND
HAMILTON MONTGOMERY, M D
ROCHESTER, MINN

THE SYNDROME of hereditary anhidrotic ectodermal dysplasia, which has as its most prominent characteristics anhidrosis, hypodontia or anodontia and hypotrichosis, is one of a group of approximately 200 primarily cutaneous congenital abnormalities that are described in Cockayne's [1] extensive study of this subject Of this group, the following five types of abnormalities were studied and described by one of us (B Y U) in a Mayo Foundation thesis, "Congenital Ectodermal and Mesodermal Dysplasias, A Clinical and Pathological Study" (1) anhidrotic ectodermal dysplasia, (2) hidrotic ectodermal dysplasia, (3) erythroderma ichthysiforme, (4) pachyonychia congenita and (5) Ehlers-Danlos syndrome

In our experience, each and all of these five types of abnormalities can well be called rare, less than 40 patients affected by them have been encountered at the Mayo Clinic in the past twenty-seven years This paper will be confined to the study of the 4 patients affected by anhidrotic ectodermal dysplasia observed at the clinic since 1920

Although, according to Darwin,[2] a description of this syndrome was given by Widderburn [3] in 1838, the term "congenital ectodermal defect" was not used until a case was reported by Christ [4] in 1913 Later observers also used this term until Weech [5] in 1929 designated the

From the section on Dermatology and Syphilology, Mayo Clinic

Abridgment of a thesis submitted by Dr Upshaw to the Faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Dermatology

1 Cockayne, E A Inherited Abnormalities of the Skin and Its Appendages, London, Humphrey Milford, 1933

2 Darwin, C R The Variation of Animals and Plants Under Domestication, New York, D Appleton & Company, 1894, vol 2, p 319

3 Widderburn, W Cited by Darwin [2]

4 Christ, J Cited by Goeckermann [14]

5 Weech, A A Hereditary Ectodermal Dysplasia (Congenital Ectodermal Defect) A Report of Two Cases, Am J Dis Child **37** 766-790 (April) 1929

and Collip[15] have reported favorably on the results of using estrogenic substances incorporated in a nasal spray in treating anhidrotic patients for chronic rhinitis or ozena In view of the normal longevity enjoyed by the patients affected by anhidrosis, the aforementioned measures, although not curative, are certainly important in making life more pleasant

REPORT OF CASES

CASE 1.—A white boy, 7 weeks of age, was brought to the clinic during warm weather because of intermittent fever that had been present since 2 weeks of age The baby weighed 6 pounds 8 ounces (2,950 Gm.) at birth and appeared normal Except for the fever of unknown origin, there were no symptoms of illness The family history revealed numerous congenital abnormalities, none of which could be related to the anhidrotic syndrome The child had no siblings, and there was no history of intermarriage of relatives

In the physical examination the only abnormal findings were absence of eyelashes and eyebrows, and very dry skin over the entire body In the hospital it was noted that the child never perspired and that his temperature increased directly in relationship to the external environment After fifteen minutes under a heat cradle, the rectal temperature rose from normal to 100 F., increases in temperature were noted after each meal No teeth were visible on roentgenologic examination Routine laboratory investigations revealed moderately severe hypochromic anemia A biopsy specimen was removed from the sole of the left foot, and the multiple sections studied revealed complete absence of sweat glands and ducts, the epidermis and cutis being normal in other respects

Four years later the mother said that no sweating had ever been noted and that by living in the basement during hot weather he had been quite comfortable and able to maintain a normal temperature At 18 months of age he had two pointed teeth which were still present and strong at the age of 4 years His scalp hair was white sparse and slow growing, he had normal eyelashes but no eyebrows The mucous membrane of his nose was dry and crusted, and he had had several severe laryngeal infections, one of which had necessitated tracheotomy His mental development was thought to be normal

CASE 2.—A white boy, 2 years old, was brought to the clinic from a warm climate by his paternal grandmother who said that since shortly after the birth of the child it had been noted that his temperature rose when he was placed in a warm environment The patient weighed 5 pounds (2,270 Gm.) at birth, six hours after this event his temperature reached 106 F. Fever continued almost constantly during the first summer, and no cause could be found When cool weather began, the child's temperature returned to normal, but it began to rise on the first warm day of the following year His pupils had been dilated since birth, they did not become smaller in the bright sunshine, and photophobia was obvious The child had had eczema of scalp, hands and feet since 6 months of age, and this was much more severe in warm weather When the teeth appeared, they were brown and fragile and soon became carious At 1 year of age, eight teeth had developed The nails had been normal until 1 year of age, when they became rough and scaly The child sat alone at 8 months and walked at 18 months

15 Mortimer, H., Wright, R. P., and Collip, J. B. Atrophic Rhinitis The Constitutional Factor, And the Treatment with Œstrogenic Hormones, Canad. M. A. J. **37** 445-456 (Nov.) 1937

The nails of anhidrotic patients are often normal but may exhibit slow growth, longitudinal furrows or slight atrophy

Delayed dentition and hypodontia regularly occur in these patients There is not only a deficiency in number of both deciduous and permanent teeth, but the teeth present are usually abnormally placed and their normal anatomic markings are frequently absent Complete anodontia accompanying anhidrosis has been reported by several authors, including Guilford [9] and Thoma and Allen [10], however, complete roentgenologic proof of anodontia is not given by all of these authors The erupted teeth, particularly the incisors and bicuspids, are often widely separated, peg shaped or conical, darkly pigmented and fragile The development of the maxilla and mandible is in proportion to the number of erupted teeth and usually depends on the amount of resulting mastication made possible, but bony development may be normal in patients with complete anodontia

We have found in the literature no reference to congenital cataracts in connection with this syndrome, although the lens is of ectodermal origin and such an anomaly might be expected Many authors, however, do report deficient function of the lacrimal glands Along with their nasal deformity, many of the patients have chronic rhinitis, often accompanied by nasal discharge of a foul-smelling fluid and diminution of the olfactory sense The glands of the mucous membrane of the nose and throat have repeatedly been found to be deficient in secretory function, producing a decrease in sense of taste, dysphagia, hoarseness and intermittent complete aphonia

Although their anomalies are of ectodermal origin, only rarely have definite defects of the nervous system been found in typical anhidrotic patients It is true, however, that numerous anhidrotic patients have been mentally inferior, but it is commonly believed that the same genetic mutation is not responsible for both of these anomalies

In addition to the aforementioned clinical characteristics which are diagnostic of ectodermal dysplasia of the anhidrotic type, other abnormalities occasionally and probably coincidentally have been associated with it, including skeletal anomalies and dysfunction of the adrenal medulla and the pituitary gland

HISTOPATHOLOGIC CHARACTERISTICS

The majority of observers who have studied excised epidermis from anhidrotic patients have reported either a total absence of sweat glands or the presence of rudimentary fragments of nonfunctioning glands and

9 Guilford, S H A Dental Anomaly, Dent Cosmos **25** 113-118 (March) 1883

10 Thoma, K H, and Allen, F W Anodontia in Ectodermal Dysplasia, [case 38], Am J Orthodontics **26** 503-507 (May) 1940

had had no convulsions at any time and had noted no aura prior to loss of consciousness The patient had been told elsewhere that he had congenital absence of the sweat glands, and he had noted heat intolerance all his life He did not relate the onset of weakness or unconsciousness to becoming overheated or to hyperventilation The family history concerning congenital defects did not disclose anything that was significant Two brothers had died in early infancy of unknown causes

Physical examination revealed a young man of average height and weight (fig 1) His forehead was extremely high, his small eyes were widely separated His nose was wide, the bridge being almost flat The lips were thick and muscular, there was total anodontia, and the mandible and the maxilla were underdeveloped, producing a "dish face" deformity

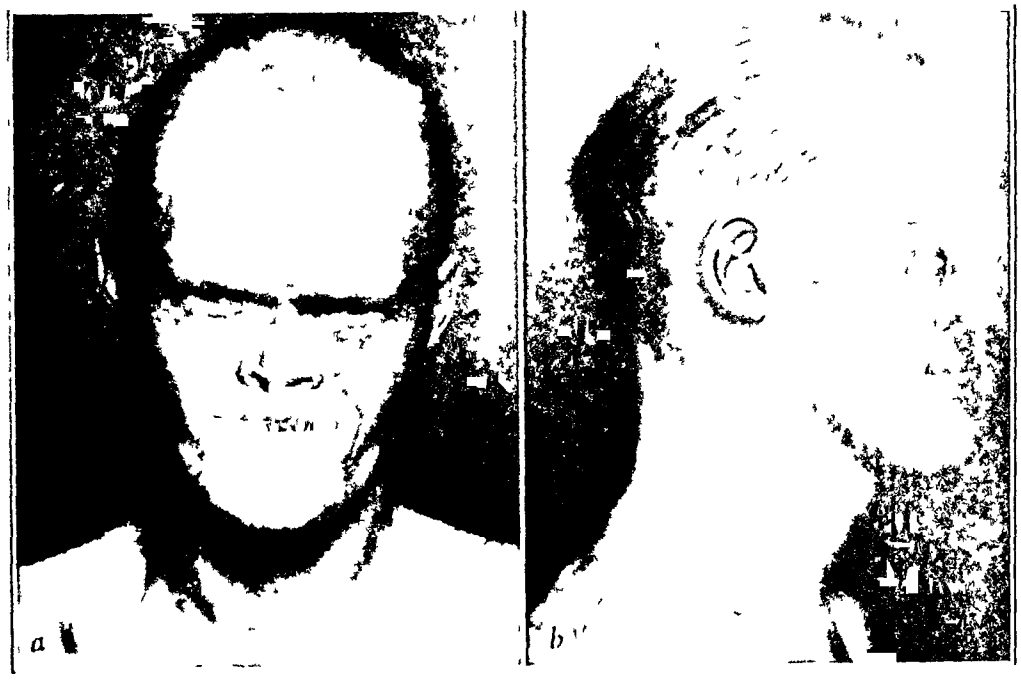


Fig 1 (case 4) —(*a*) Anterior and (*b*) profile views This is the characteristic concave facies of hereditary anhidrotic ectodermal dysplasia Note the sparse growth of hair on the scalp and the normal amount of lanugo in the shoulders

No activity of sebaceous or sweat glands was noted anywhere on the skin, which was excessively dry A diffuse symmetric keratoderma covered the palms, the soles and the nails were normal

There was considerable alopecia of the scalp, most prominent over the vertex The scalp hair present was stiff and dry, and only a few hairs were present anteriorly Eyelashes and eyebrows were absent, and only a few sprigs of hair were present in the axillary and pubic regions The beard was normal, as was the lanugo on the thorax and the shoulders, but lanugo was absent elsewhere

The mammary glands were absent, and there was no pigmentation to mark their usual site No teeth were present The eyes and the lacrimal glands were normal

The thin septum of the nose contained no cartilage, and the mucous membrane was atrophic The senses of smell and taste were intact

ETIOLOGIC FACTORS

Because of the facial similarity of anhidrotic patients and patients with congenital syphilis, clinicians formerly believed the cause of the anhidrotic syndrome to be congenital syphilis Still others explained the syndrome on the basis of endocrine dysfunction, but it now appears that all etiologic concepts other than those of heredity have been disproved

The first anhidrotic patients described by Widderburn,[3] were 10 male members of a Hindu family, and although many patients have been reported who gave absolutely no family history of abnormalities, the majority of patients have ancestors with similar anomalies When the full syndrome is not found in other members of the family, several of them will often have one or more of the component anomalies, except anhidrosis, that comprise typical anhidrotic dysplasia

The exact mode of genetic transmission of the full anhidrotic syndrome has been the subject of controversy since the first cases were encountered It was noted early that males are affected much oftener than females, of the first 60 patients, only 8 were females, according to Kaalund-Jørgensen and Christensen,[6] who also listed 7 instances in which the typical syndrome occurred in siblings Wechselmann concluded from his studies that the defect was transmitted as a sex-linked characteristic, in the same manner as hemophilia, by an unaffected female conductor to affected male members of the family [13] Goeckermann,[14] in a report on a female patient, pointed out that the syndrome was not always recessive in females As more and more cases were reported, it became obvious that the mode of genetic transmission is not identical in all patients Geneticists now emphasize that one peculiarity of human genetics is that the same abnormal character may be sex linked, dominant or recessive in different families, and there are now reports in the literature of the genetic transmission of the complete anhidrotic syndrome by each of these modes of inheritance

PATHOGENIC FEATURES

Although the time and mode of production of the anhidrotic syndrome constitute a subject of much speculation, little detailed information is known

The relative order of normal embryologic development of the dermal appendages which are involved in the syndrome is as follows 1 The hair develops from downgrowths of the epidermis which appear

13 Wechselmann, W, and Loewy, A Untersuchungen an drei blutsverwandten Personen mit ektodermalen Hemmungsbildungen, besonders des Hautdrusensystems, Berl klin Wchnschr **2** 1369-1373 (July) 1911

14 Goeckermann, W H Congenital Ectodermal Defect, with Report of a Case, Arch Dermat & Syph **1** 396-412 (April) 1920

COMMENT ON CASES

As in case 1, it is not uncommon for anhidrotic infants who have increased temperature shortly after birth to be extensively and vainly studied for evidence of infections Seldom is the correct diagnosis made in the first few weeks of life, and so the child is not subjected to varied and multiple therapeutic methods In contrast to those in adults, the obvious clues to the correct diagnosis, namely, anodontia and hypotrichosis, are normal findings at this age The typical anhidrotic facies, although observed as early as 1 year of age, is not conspicuous in the first few weeks of life, and in the absence of a history of similar hereditary anomalies, unless the family or the physician notes that the rise of temperature is correlated with the external environment, the diagnosis may be delayed until lack of teeth and hair is noted in the second six months of life In case 1, since the patient fortunately was examined in August, the correlation of high body temperature and high external environmental temperature was noted, when, in further study of this phenomenon, the patient was exposed to a heat cradle and no sweating was produced at an abnormally high body temperature, only the biopsy showing absence of sweat glands on the sole of the foot was needed to confirm the diagnosis The absence of teeth on roentgenologic examination of the mandible and the maxilla was further evidence of the existence of the complete anhidrotic syndrome In the child's subsequent development, the repeated infections of the upper part of the respiratory tract illustrated one of the common complications resulting from the abnormal formation of the mucous membrane

Of particular interest in case 2 were the pupillary abnormalities and the mode of inheritance of the syndrome, the latter factor being unknown in case 1 The inability of the pupils to respond to any type of physical or chemical stimuli was thought to be due to defective innervation, though the site of this abnormality of the nervous system could not be determined in absence of other neurologic signs or symptoms This anomaly appears to be one of the rare examples of abnormalities of the nervous system that accompany the complete anhidrotic syndrome

In case 2 all of the patient's manifestations of anomaly were said to be duplicated in his only sibling, a sister, 8 months old When one remembers that the children's parents had common great-grandparents each of which may have carried the anomaly as a recessive genetic character, it is easy to understand why marriage between their descendants resulted in defective children These are obviously homozygous for the causative gene, and this recessive gene was concealed

TREATMENT

Treatment of anhidrotic patients is largely symptomatic because of the fundamentally aplastic lesions of the syndrome, but certain therapeutic principles should be emphasized to the patient or to the parents of an anhidrotic infant The limiting effect of the anhidrosis on the mode of living must be well understood, the genetic transmission of

Differential Diagnosis of the Anhidrotic Syndrome

	Anhidrotic Ectodermal Dysplasia	Hidrotic Ectodermal Dysplasia	Werner's Syndrome	Rothmund's Syndrome	Proge Hutchi Gulliford
	Dominant, recessive or sex linked	Usually dominant	Usually recessive	Usually recessive	Not prov
of	First year	First year	20 to 30 yr	1 to 5 yr	1 to 5 yr
	Inverted pyramid, frontal bosses, depressed nasal bridge	Not characteristic	Senile changes, beaked nose, small mouth and chin	Not characteristic	Frontal b beaked n retracted
	Dry, soft, feminine	Hyperkeratoses of palms and soles, oriental pigmentation	Epidermal, subcutaneous and muscular atrophy of distal extremities with trophic ulcers	Atrophy, brownish pigmentation, telangiectases	Atrophy epidermis cutaneou and mus
us	Markedly decreased	Slightly decreased	Normal	Normal	Normal
lands	Decreased or absent	Normal	Normal	Normal	Normal
ry	May be absent	Normal	Normal	Normal	Normal
	Generalized alopecia, usually subtotal	Generalized alopecia, always subtotal, fragile hair	Canities and premature alopecia	Usually normal	Premature alopecia
	Normal	Short, thick, elevated tip	Normal	Normal	Short, fra
	Decreased or absent, also deformed	Normal	Normal	Normal	Irregular developm
	Normal	Normal	Juvenile cataracts	Juvenile cataracts	Normal
or					
scular	Distinct intolerance of heat	None	Early arteriosclerosis	None	Early arterioscl
	None	Usually none	Short stature, osteoporosis	Occasionally short stature and small hands and feet	Dwarfed tr and extre joint defo
e	Usually none	Pituitary and suprarenal deficiency (?)	Hypogonadism, diabetes	Occasional hypogonadism	Hypogona
r life	About average	Average	Death before age of 40 yr	Average	Death befo age, of 30

the defect should also be explained, and no assurances should be given to the parents of an anhidrotic child that future children will be normal

Artificial dentures should be fitted early in anhidrotic children with hypodontia to facilitate the development of the mandible and the maxilla Plastic repair of the saddle nose deformity will likewise do much to improve the patient's facies and general morale Mortimer, Wright

SUMMARY

The clinical characteristics of hereditary anhidrotic ectodermal dysplasia are described, emphasis being placed on the diagnostic triad of symptoms anhidrosis, hypodontia and hypotrichosis The most important dermatopathologic abnormality, complete or almost complete lack of formation of sweat glands, is pointed out, along with its effect on the patient's heat-regulating mechanism The several modes of hereditary transmission of the syndrome, as well as the embryologic development of the anomalies, are discussed The essential similarities and differences between the anhidrotic syndrome and hidrotic ectodermal dysplasia, Werner's syndrome, Rothmund's syndrome and the Hutchinson-Guilford type of progeria are pointed out in tabular form Four patients who were affected by the anhidrotic syndrome, 2 of them infants, are reported on in detail The report includes physiologic investigations of sweating, histopathologic examinations of epidermal tissue and inquiries regarding the genetic transmission of the anhidrotic syndrome in each patient's family group There is need that the syndrome be recognized promptly, particularly in an infant, so that the child may not be exposed to a warm environment and, as his development progresses, may have the benefit of dental prostheses early enough to prevent some of the facial abnormality which results from uncorrected hypodontia or anodontia

The family history revealed no congenital abnormalities, but the patient's paternal great-grandfather and maternal great-grandmother were brother and sister The patient's one sibling, a sister of 8 months of age, was said to have the same abnormalities of eye and temperature as were noted in the patient

On physical examination, the child appeared to be well developed and nourished The facies and the hair distribution were not unusual, but the skin was dry, and no sweating was noted No eczematoid lesions were present, and the teeth and nails were as described The pupils were equal and semidilated and did not react to light Pupillary dilatation did not occur after local instillation of homatropine hydrobromide nor constriction after instillation of physostigmine salicylate or a pilocarpine salt There were pupillary remnants in both eyes, and the fundi were normal The remainder of the physical examination revealed no significant findings, and the laboratory examinations gave essentially normal results

Further observations of the child revealed that his temperature increased after eating and with crying but could be easily controlled by sponging him with cool water After administration of pilocarpine there was flushing of the face, neck and breast down to a sharp line at the nipple level, but no sweating occurred Biopsy of the skin was not performed

When the patient was 5 years old, the grandmother stated that he still was intolerant to heat, that there was no change in his pupils and that his deciduous teeth were black stumps except his six year molars, which appeared normal No sweating had ever been noted in the patient's younger sister, and although she had a complete set of deciduous teeth, they were darkly pigmented and sensitive to sweets, heat and cold

Case 3.—A white man, 26 years of age, unmarried, working as lifeguard, first came to the clinic during warm weather because of lack of perspiration, scanty growth of hair and abnormal dentition These abnormalities had been present since birth, and the father stated that the patient's abnormalities were familial in character, originating many generations ago in the patient's mother's family, always appearing in one male of each generation and completely absent in the women of the family as far as he knew

Physical examination revealed a well nourished man of average adult size, the ears were protuberant, the root of the nose was depressed and the septum was irregular, but there was no widening or saddle nose deformity The skin was soft and dry On the scalp there was only a sparse peripheral fringe of hair, there was little lanugo over the trunk and extremities, and only a few small tufts of hair in the pubic and axillary regions Two teeth were present, one of which was a small tag There was moderate atrophy of the mucosa of the nasopharynx, pharynx and larynx, but the voice was normal

Biopsy and other laboratory procedures were not performed until the patient was admitted to the clinic a second time, five years later Then it was found that after strenuous physical exercise the rectal temperature increased 2 degrees F His basal metabolic rate was normal on two occasions, but after strenuous exercise it increased to + 40 per cent, while the metabolic rate of the normal control person increased to + 20 per cent After his second admission, histologic examinations were made of skin tissues removed from the right axilla and the lower right part of the thorax, in the serial sections no trace of hair follicles, sebaceous glands, sweat glands or apocrine glands could be found

Case 4.—A 23 year old unmarried farmer came to the clinic because of weakness of the arms and legs and loss of consciousness, usually occurring just preceding a meal or several hours afterward These symptoms began suddenly during one hot day of the preceding summer and continued to recur during cooler weather He

The Rev Walter Calton (1850), in his book "Three Years in California,"[2] described the continued annoyance caused by fleas to strangers and observed that the native was not troubled by them

Carl Meyer (1855), under the title "Nach dem Sacramento,"[1] described a night spent on a ranch near Salinas He labeled his experience "flea fever"

Hardly has one gone to bed when a band of these small devilish fleas pursue their bloody maneuvers on one's sensitive skin, driving away sleep and tormenting a man to madness One breaks out in a torturing sweat, and because of the frequent throwing off of the covers one runs a risk of contracting a fever

He mentioned that even in mixed company the subject of fleas was often the topic of conversation and that the gesture of scratching was not frowned on

Ernest de Massey wrote in his "Frenchman in the Gold Rush"[1] of his experiences in San Francisco

There were millions of fleas in the sand near my shack On the floor was a layer of sand, the camping ground of a colony of fleas, which hopped around looking for a chance to make a good meal off me [and] by the time I was ready to retire my legs were literally covered with these blood thirsty insects

Frank Marryat, an Englishman, in his "Mountains and Molehills"[1] described his experiences in Santa Rosa, Calif On being shown his quarters he was "immediately attacked by the fleas with a vigor which was perfectly astonishing" He had been a wide traveler and had "been tortured by sand fleas in the Eastern Archipelago and by all kinds of mosquitoes from Malta to Acapulco," including the "famous 'tiger' breed against which there is no recourse but flight" "But," he said, "I would have preferred any of those annoyances to the attack of those Santa Rosa fleas" "The place was alive with them and they, raised in the rough school of the wild bullocks' hide, boldly faced as they attacked us" He stated that, on his mentioning the fact, his host predicted that he would get used to the fleas that he [the host] and his family never gave them a thought Thus the early settlers in California had observed that one became immunized against the effect of flea bites by being bitten by the fleas

In the San Francisco *Argonaut* of Dec 8, 1878,[1] there appeared a humorous article with the title "The Flea A Short Discourse on a Lively Subject" The author gave an account of his experiences with fleas encountered near what is now Redwood City At that time it was believed that fleas lived in the soil The author chose a site for his

2 Calton, W Three Years in California, New York, A S Barnes & Co, 1850, p 70

Routine examinations of blood and urine gave normal results, as did determinations of the basal metabolic rate and the fasting blood sugar, calcium and potassium Roentgenograms of the skull and the thorax did not disclose any abnormality, and the electroencephalogram revealed mild generalized dysrhythmic activity without localizing signs

Under an electric baker the patient's oral temperature rose from 98 2 to 100 4 F in fifteen minutes After an injection of 5 mg of furfuryl trimethylammonium iodide (furmethide®) flushing and weakness were noted, but no sweat, and no tremor or unconsciousness developed

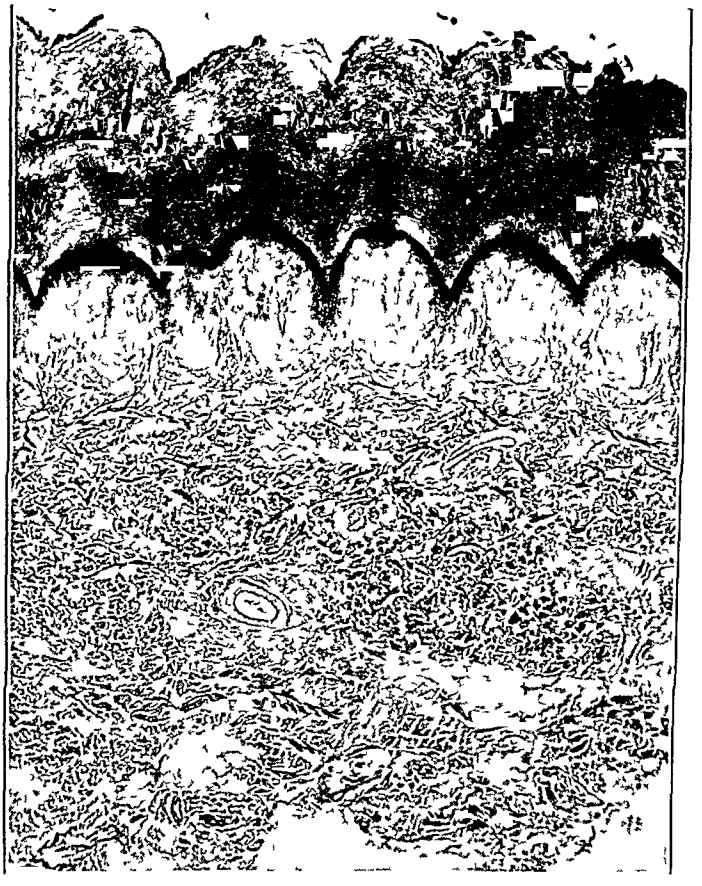


Fig 2 (case 4) —Section of a biopsy specimen removed from the palm It shows complete absence of sweat glands and ducts (hematoxylin and eosin, × 25)

Biopsy specimens were removed from the skin of the right forearm, right arm and palm of the right hand, in the serial sections no trace of coil glands or ducts was visible (fig 2)

Over a period of several months, three plastic procedures employing cartilage implants succeeded in forming an elevated nasal bridge, so that the patient's appearance was improved Diphenylhydantoin sodium (dilantin sodium®) was prescribed in an attempt to control the episodes of weakness and unconsciousness, the patient was advised to restrict his strenuous farming activities during hot weather

The length of time required for each developmental stage is very largely determined by the prevailing temperature and humidity Adult fleas may remain alive for more than five years if the environmental conditions are favorable, such extremely long adult life is, of course, very exceptional, usually the flea lives only a few weeks or months Because of the lack of extremes in temperature and the relatively high humidity, in coastal California fleas breed the year around They are found in homes where cats and dogs are kept as pets, particularly in the carpets and cracks of floors and corners of rooms They are found in basements where the animals sleep at night They are particularly apt to be found in large numbers in such basements from which the usual animal



Fig 1—Cat flea (Courtesy of Morris A Stewart, Ph D, Department of Entomology, University of California, Berkeley, Calif)

and human tenants have been absent for a period I know of persons who have walked into their own basements after a summer vacation, to have their white trousers literally covered with very hungry fleas in a few seconds Fleas also frequent outhouses, sand piles and lawns and such places as theaters I know of people who are bitten by fleas whenever they attend any theater

CLINICAL PICTURE

The typical clinical picture of reaction to flea bites is a grouped, itching, urticarial, papular eruption, some papules of which contain a central red punctum (fig 2) These lesions are most often found along the

until the consanguineous marriage by a dominant normal gene, that was absent in these two children Progeny of heterozygous parents would be expected to show a 1 3 ratio of defective to normal children, but this ratio often becomes apparent only in large families or in long family pedigrees

In case 3 a sex-linked recessive gene was responsible for the defect, according to the father of the patient, since only one male of each generation was affected In contrast, in case 4 we were unable to trace the anomaly at all One must conclude that the condition in this case represents a mutation, and the patient's progeny should be followed with interest to note the genetic transmission of the defect

The facies of the 2 adult anhidrotic patients (cases 3 and 4) is characteristic of the entire group Although in case 3 the patient did not have a saddle nose such as that described in case 4 and frequently described in the literature, the root of his nasal bridge was sharply depressed Both patients presented decided hypotrichosis, complete anhidrosis and hypodontia or anodontia to complete the full anhidrotic syndrome

The anhidrotic syndrome had limited the heat regulation in case 3 to such an extent that the patient's employment as a lifeguard was one of the few types of work which he could carry on in the summertime In case 4 the patient's activity was voluntarily restricted, but he was able to continue farm work in a northern state during almost the entire year We were unable to relate the cause of his periods of weakness and unconsciousness directly to increase in body temperature, but it was felt that a subthreshold cerebral dysrhythmia was made manifest either by the rise in temperature or by the hyperventilation or by both factors

These patients (cases 1, 3 and 4) were all of interest from the standpoint of histopathologic study In none of their biopsy specimens were we able to find sweat glands or sebaceous glands In case 3 the apocrine glands were also absent from the axillary skin examined This is in contrast to the reports of Sunderman,[11] whose patients had apocrine glands but no eccrine glands, as shown by microscopic examination The apocrine glands develop from anlages of hair follicles instead of directly from the epidermis as do sweat glands, in the embryo, and do not become active until near puberty The presence of highly developed apocrine glands and the sparse growth of hair, on one hand, and the absence of sweat glands, on the other, illustrate the complete suppression of the sweat gland formation and the incomplete suppression of pilosebaceous structures which are peculiarly characteristic of the anhidrotic syndrome

by the flea as he bites Or, to put it in other words, a flea may bite, and as a result there may be urticarial lesions at sites remote from the bitten areas

The history is equally important If the sufferer is adult, he is usually new to the Bay region He has been subject to flea bites for only a sufficient period of time to become sensitized by the antigen Most patients suffering from flea bites are children, newly born or newly arrived in the Bay area

Other types of eruptions which are seen more rarely are secondary bacterial infections and other complications of scratching Recurrent



Fig 4—Typical flea bites Note resemblance to papular urticaria (Courtesy of Samuel Ayres Jr, M D, Los Angeles)

furuncles, especially in children, have been observed Less frequently occur bullous eruptions on the lower extremities and generalized, erythema-multiforme-like, bullous eruptions

DIFFERENTIAL DIAGNOSIS

It is the experience of those in our office that most cases diagnosed as "papular urticaria" in our district are in reality examples of flea bites Chipman [4] recognized this fact long ago While my associates and I do

4 Chipman, E D Urticaria, with Special References to the Cause in the Papular Forms of Children, California State J Med 8 207 (June) 1910

FLEA PROBLEM IN CALIFORNIA

C J LUNSFORD, M D
OAKLAND, CALIF

THE TESTIMONY of present day dermatologists is that fleas are more of a nuisance in California, particularly in the San Francisco Bay area, than elsewhere in the United States

HISTORICAL ACCOUNTS

In the vast literature relating to exploration, settlement and life in California the references to misery caused by fleas encountered by the authors are related entirely to experiences in Northern California

Padre Juan Crespi,[1] the diarist of the Portola expedition of 1769, wrote that when the expedition visited an Indian village on Purisima Creek in San Mateo County they found the grass huts so infested with fleas that they called it "Village of the Fleas"

In 1786 the Frenchman La Perouse [1] had this to say about the fleas in Carmel and Monterey "Under the influence of the Missionaries the Indians had refused to make the slightest change in the construction of their huts because they could set fire to their huts when the fleas became a pest and could rebuild them in two hours"

Another Frenchman, Duhart-Lilly (1827-1828) [1] visited a ranch in the San Bruno Valley Concerning the sleeping arrangements he wrote, "We were compelled to stow ourselves away, guests, husband, wife and children all together, upon a great feather bed, where devoured by fleas we passed quite an uncomfortable night"

In the period of transition from Mexican sovereignty to that of the United States, the American Edwin Bryant, in his outstanding book, "What I saw in California," [1] wrote bitterly and in detail of the infestation of the rancheros and old missions with fleas He spoke of the missions as "nurseries of fleas" "If any sinning soul ever suffered the punishment of purgatory these torments were endured by myself last night," he said After a sleepless night there was no square inch of his body that was free from flea bites

Read at the Sixty-Eighth Annual Meeting of the American Dermatological Association, Inc, San Diego, Calif, April 28, 1948

1 The Flea in California History and Literature, California Hist Soc Quart **15** 329 (Dec) 1936

urticaria is an allergic manifestation, the exciting cause of which is associated with home sleeping arrangements and can be controlled by detaining the child in the hospital for the night only Kinnear [8] described 14 cases of papular urticaria in children which began on their arrival in England from America and said that other cases occurred in their families He had also observed that same occurrence in newly arrived medical students He agreed with Hallam [6] that this condition had something to do with home sleeping conditions He had no idea of the cause and made no mention of the possibility of flea or other insect bites Tate [7] said, "The exciting agent is something connected with the patient's home environment"

My associate, Dr H J Templeton,[11] personally observed many cases of "papular urticaria" in Vienna He reported that patients with so-called papular urticaria suffered from typical flea bites and that their lesions would have been so diagnosed by any of the West Coast dermatologists He observed this "papular urticaria" developed in members of his own family and also in persons in the families of other American physicians and that the lesions were typical flea bites That the diagnosis was not shared by all Viennese dermatologists is evidenced by Dietrich's [12] discussion in which he stated that the cases were really examples of insect bites It is my belief that this confusion occurs in many cases in the literature

Urbach [13] devoted eight pages to the idea that most cases of papular urticaria are of allergic, endogenous or gastrointestinal origin and only two lines to cases in which insects were the cause His photographs 347 and 353 [13] are highly suggestive of bites In another text [9] he showed a photograph of papular urticaria which looks to me like insect bites Macleod's text [14] has a photograph which is almost certainly one of flea bites, with the puncta, papules, grouping and location A photograph in Andrews' text [15] needs to be differentiated from one of flea bites At a clinical meeting of the American Dermatological Association [16] a 3 year old child was presented from Canada as having an example of papular urticaria In the discussion Ayres and Weiss diagnosed the

11 Templeton, H J Personal communication to the author

12 Dietrich, A Lichen urticatus exogenes, Wien klin Wchnschr **50** 1730 (Dec 17) 1937

13 Urbach, E, and Gottlieb, P M Allergy, New York, Grune & Stratton, Inc, 1943, pp 884-891

14 Macleod, J M H Diseases of the Skin, New York, Paul B Hoeber, 1924, p 698

15 Andrews, G C Diseases of the Skin, Philadelphia, W B Saunders Company, 1930, p 348

16 King-Smith, D, Trow, E J, and Dixon, H A Urticaria (Papular), Arch Dermat & Syph **25** 172 (Jan) 1932

home near a ranch called "Rancho de las Pulgas," where the beauty of the country impressed him He observed that potatoes planted in the soil had to be removed with a crowbar because of the hardness of the soil and that the potatoes when dug were as "flat as pancakes" He thought that fleas could not live in such soil On calling on the owner of the ranch he noticed a stick ladder leading from the floor to a high attic under the roof, where the household slept The significance of such an arrangement became apparent when, on being severely bitten about his ankles, he looked down and saw that his white socks were covered with "pepper in motion" The home owner then told him that his routine for sleep was to remove all his clothes, leave them on the floor and scurry up the ladder, leaving only the clothes for food for the fleas Subsequently the author learned that "Rancho de las Pulgas" signified "The Farm of the Fleas"

ENTOMOLOGY OF FLEAS [3]

The three species of fleas most commonly attacking man in the United States are the human flea (Pulex irritans), the cat flea (Ctenocephalides felis) and the dog flea (Ctenocephalides canis) In the eastern part of the United States the dog flea is the dominant pest In the South and West the human flea is In California the human flea and the cat flea are equally dominant (fig 1)

The eggs of all these species hatch in the nests or resting places of their hosts, rarely on their bodies, or else in dust or organic debris in buildings Following the life cycle of any insect, from egg to larva to pupa within the cocoon, the adult flea emerges in about two weeks Newly emerged adults are usually very fat and can live for several months, under favorable conditions, without feeding The female flea must have a blood meal before her eggs can be fertilized Most fleas visit the body of the host for relatively short periods for the purpose of obtaining a blood meal

On smooth surfaces, fleas progress by means of short jumps They may sham death when disturbed They usually leave a dead host as soon as the body becomes cold They like warmth and moisture but shun daylight It has been determined that some adult fleas can jump vertically nearly 8 inches (20 cm) and horizontally 13 inches (33 cm) Fleas prefer hosts with nests

The life cycles of fleas are decidedly influenced by meteorologic factors Low atmospheric humidities in particular are inimical to them

3 The data and some of the phrasing on entomology were given to me by Morris A Stewart, Ph D , Professor of Parasitology, the Division of Entomology and Parasitology, University of California, Berkeley, Calif

in a lymphocytic infiltration around the blood vessels, which were dilated and often filled with the lymphocytes The same lymphocytic infiltration occurred around the sweat and sebaceous glands and, in 1 case, around the muscle fibers In three of the specimens there was a very pronounced lymphocytic infiltrate around the sweat glands deep in the corium and even as deep as into the fat layer (fig 6) I was impressed by the intensity of this deep lymphocytic reaction

DATA OBTAINED FROM OUR LETTERS OF INQUIRY

In the fall of 1947 my associates and I mailed letters to all certified dermatologists in the United States, Canada, Hawaii and Cuba, asking about the flea problem in their communities

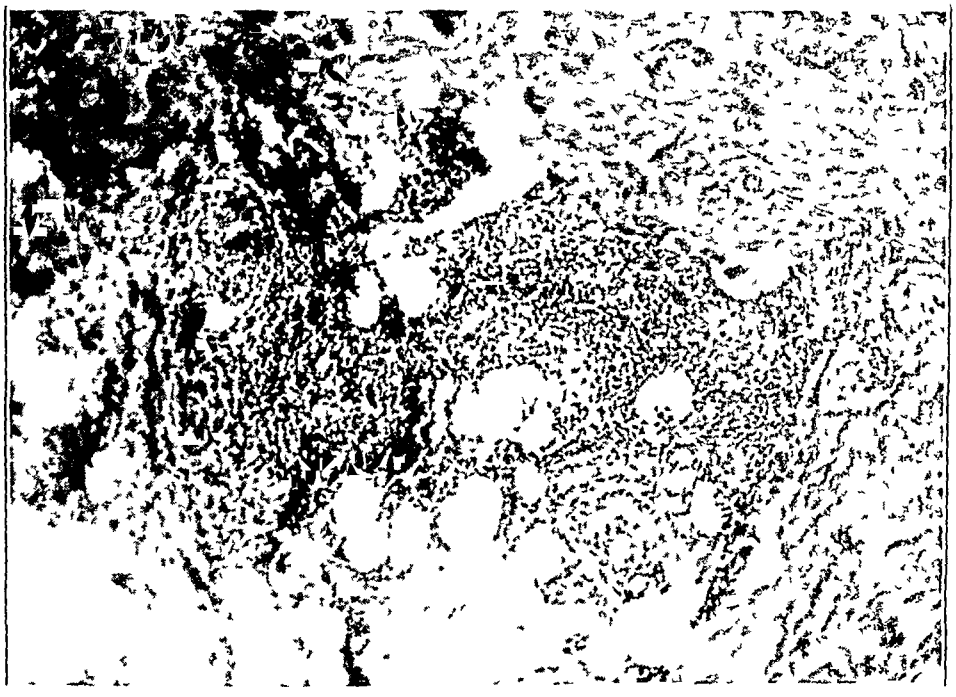


Fig 6—Histologic changes seen in the flea bite Note the intensity and the depth of involvement in the fat layer

The data in the letters received showed that fleas are a major dermatologic problem only in California Of the several hundred answers from all other parts of the country only a few persons gave as their opinion that fleas were a major medical problem in their community A slightly larger, but still small, percentage of letters stated that fleas were a minor problem In two states, Nevada and Colorado, some observers denied that cat and dog fleas even existed there

In California, however, in all letters from the San Francisco Bay area there was agreement that a real problem exists In eight letters from Los Angeles four dermatologists stated that the problem exists and four denied it All six letters from the Los Angeles suburbs contained statements that a moderate problem exists From the San Diego

waist line and on the hips and shoulder area, where the clothing fits snugly (fig 3) They may, however, be on any part of the body Grouping is one of the most characteristic features The flea is not content to bite in one area and remain attached at that point until its hunger is satisfied Rather, it moves along, biting in an irregular but grouped



Fig 2—Individual flea bites, showing papules, central puncta and vesiculation



Fig 3—Flea bites in typical round the waist distribution (Courtesy of Rees B Rees, M D, San Francisco)

pattern In addition, there may be more scattered or satellite lesions present In some cases a generalized papular urticaria is seen (fig 4) It is believed that many of such papules are allergic reactions to one or a few bites and are an expression of sensitivity to the antigen injected

COMMENTS AND STUDIES ON IMMUNOLOGY

The entomologists say that the old idea of host specificity is erroneous Persons who think they are not bitten by fleas from their own dogs actually may have been bitten until they have established an immunity Also, *some persons not bothered by fleas at home may be sensitive to* a slight variation in antigen from fleas in a strange city

It appears that as a person continues to be bitten he undergoes a natural desensitization to the antigen deposited by the flea This takes place gradually over a period of about a year There are people, however, in whom this desensitization occurs more slowly, and in some cases it never occurs Patients have been known to leave the Bay region permanently because the fleas have made their lives intolerable

The biologic explanation for the phenomenon of natural desensitization against insects is illustrated by an experiment done by Kenneth Mellanby [21] To study the varying reactions to insect bites in man he fed the yellow fever mosquito on Englishmen who had never been away from the British Isles The first bites produced an erythema about 1 to 2 mm in diameter and in twenty-four to forty-eight hours a delayed reaction consisting of an intensely pruritic urticaria-like papule 1 cm in diameter surrounded by a 2 to 3 cm zone of redness After the subjects had been bitten for a month the immediate reaction was an itching wheal which was followed by the delayed reaction in twenty-four to forty-eight hours The later reaction recurred each three to four days As the experiment continued the delayed reaction gradually disappeared and there was less itching, but the immediate reaction never failed to appear Dr Mellanby stated, however, that many Englishmen bitten by thousands of indigenous mosquitoes finally lost the immediate reaction and had complete desensitization He expressed the opinion that the two reactions were quite distinct and were caused by different antigens in the saliva of the mosquito

My associates and I believe our clinical observations tend to show that a similar process of desensitization occurs naturally on prolonged exposure to flea bites

In 1939 Cherney, Wheeler and Reed [22] tested two groups of persons to an antigen made from dog, cat and human fleas *indigenous to* San Francisco About 85 per cent of the immune group gave no reactions A number of susceptible persons were given weekly injections for six weeks with the flea antigen in an attempt at desensitization The results of treatment were fair

21 Mellanby, K Man's Reaction to Mosquito Bites, Nature, London **158** 554 (Oct 19) 1946

22 Cherney, L S , Wheeler, C M , and Reed, A C Flea-Antigen in Prevention of Flea Bites, Am J Trop Med **19** 327 (July) 1939

not deny the existence of true papular urticaria of endogenous origin we are certain that it is rare in comparison with the exogenously flea-produced variety Children, particularly, or adults who are newcomers to the Coast are sometimes referred to us by pediatricians or general physicians, with the diagnosis of "hives" The story will invariably be that the patient had not been subject to hives prior to coming to the Coast and that the eruption appeared shortly after arrival here Usually the physician or the patient considers the condition to be an allergy to some of the foods of the West Coast, such as sea foods or fruit It takes a great deal of persuasion for one to convince these patients that the origin of the eruption is not what they are eating but, rather, what is eating them Although this fact is known to all the local dermatologists, it is astonishing that it is not known to all physicians and to the laity

This failure to recognize such a simple, obvious thing as flea bites is not limited to our locality The Jadassohn [5] school in Germany, Hallam,[6] Tate,[7] and Kinnear [8] in England and Urbach [9] in Vienna reported that papular urticaria in children disappeared when the patients were hospitalized and recurred when they returned home Reasoning from this information the English observers [10] and Urbach [9] expressed the conclusion that papular urticaria is an allergic manifestation, the exciting cause of which is something in the home environment, food or bedding These authors made little or no mention of the possibility of fleas or other insects being etiologic factors One of Jadassohn's pupils, Gerard Simon,[5] described a case of prurigo which cleared while in the hospital and had an exacerbation when the patient returned home Hallam [6] quoted Jadassohn to the effect that he had noted many years ago that cases of Hebra's prurigo cleared up when the patients were hospitalized Although the evidence against fleas in these older reports is uncertain, the possibility should be considered In recent reports the evidence against fleas is much stronger Hallam [6] reported a series of patients with papular urticaria whose condition cleared on hospitalization only to relapse on their return to their homes He concluded that papular

5 Simon, G Beitrage zur Kenntniss der "Neurodermitiden," Bern, Stampfli & Co, 1898

6 Hallam, R Further Observations on the Aetiology of Papular Urticaria (Lichen Urticatus), Brit J Dermat & Syph **44** 117 (March) 1932

7 Tate, B C Papular Urticaria (Lichen Urticatus), Arch Dis Childhood **10** 27 (Feb) 1935

8 Kinnear, J Urticaria Papulosa, Brit J Dermat & Syph **45** 65 (Feb) 1933

9 Urbach, E Skin Diseases and Nutrition, Including the Dermatoses of Children, Vienna, Wilhelm Maudrich, 1932, p 175

10 Hallam [6] Tate [7] Kinnear [8]

EXPERIMENTS

With Normal Conditions—EXPERIMENT 1 The fleas were fed on 12 members of our office staff and their families All except 1 were old residents of the Bay region The exception had been reared on a ranch and knew that she had been exposed to fleas all her life Although the fleas fed with equal avidity on all 12 subjects, only 2 persons showed a positive reaction Both of these had been flea-sensitive all their lives The reactions were both immediate and delayed This experiment demonstrates the immunity of 10 out of 12 old time Californians to flea bites

EXPERIMENT 2—Fleas were fed on 8 volunteer students at the University of California in Berkeley, none of whom gave a history of previous sensitivity to fleas Of the 7 that returned for observation only 1 had been a resident of the San Francisco Bay region for longer than two months The exception had lived here for six months Seven of the 8 volunteers showed a positive delayed reaction at the end of forty-eight hours This experiment indicates the sensitivity of recent residents in the Bay region to flea bites

EXPERIMENT 3—Fleas were fed on 4 bottle-fed newborn babies at the Highland-Alameda County Hospital None of the babies had been out of the hospital At the end of forty-eight hours there had been no reaction This experiment indicates that persons on first being bitten by fleas are not sensitive to their bites

With Local Application of Repellents—Oil of Citronella Two of our nurses applied oil of citronella to their forearms The fleas were repelled and did not feed It was interesting to see them dance all over the feeding ground

Pyrethrum Two subjects had powder containing 0 7 per cent pyrethrum dusted on their forearms In 1 case the fleas fed In the other the fleas were repelled after five minutes of feeding In both instances fleas were listless for twenty-four hours and would not feed but recovered In 2 other subjects other fleas were exposed to a heavier powder sprinkling Although we did not see them feed, they all died in twenty-four hours

Army 612 (2-ethyl-hexanediol-1, 3) Three subjects were tested The fleas were repelled, and most died within twenty-four hours

DDT Powder (7 5 per cent DDT) Two subjects were studied The fleas would not feed after five minutes and died in four hours We did not pursue this experiment because we could not afford to kill more of the fleas

Camphor Spirits of camphor was applied to the forearms of 6 subjects, and fleas were placed thereon The fleas would not feed One volunteer forgot to cleanse the camphor from his forearm properly Four hours later two tubes of fleas were fed on the same site The fleas were dead in fifteen minutes

Petrolatum In four instances fleas would not feed through petrolatum rubbed on the forearm

With Internally Administered Repellents—Sulfur Four patients were fed calcium sulfide, ¼ grain (15 mg) twice a day for seven days Fleas fed normally and were not made ill We have been advised that farmers in certain parts of the country, believing that sulfur will protect them from fleas, take it in the spring for that purpose

Quinine Eight tubes of fleas were fed on 4 subjects given 5 grains (0 30 Gm) of quinine sulfate three times a day for three days At the end of thirty-six hours 90 per cent of the fleas were dead

Thiamine Hydrochloride One subject was given 100 mg of thiamine hydrochloride, intramuscularly One half hour later the fleas fed Six hours, ten hours

case as one of insect bites In the *British Journal of Dermatology and Syphilis* [17] a reviewer wrote of "papular urticaria (a condition furtively believed by not a few since Jonathan Hutchinson to be produced by insect bites) " Jonathan Hutchinson [18] expressed the opinion that fleas had something to do with the lesions "It may be that flea bites acting on a skin sensitized by faulty alimentary metabolism is the determining cause" Concerning the first step in treatment MacKenna [19] said, "Inquire judiciously into the possibility of infestation with fleas"

From all this evidence, I conclude that elsewhere in the world there is the same problem of differentiating papular urticaria from flea bites that exists on the West Coast



Fig 5—Histologic aspects of the flea bite Note the intensity of the reaction

PATHOLOGIC ASPECTS

A flea bite papule was excised from each of 5 patients for microscopic examination Each of these lesions was of the papular urticarial variety most commonly seen as the result of flea bites None was of the rarer bullous variety

In none of the excised specimens was there any significant change in the epidermis Most of the abnormal observations were in the subpapillary and deeper portions of the corium (fig 5) These consisted

17 Hartman, M The Use of Hormones in Dermatology, Brit J Dermat. **60** 30 (Jan) 1948

18 Hutchinson, J , cited by MacKenna, R W Diseases of the Skin, ed 3, Baltimore, William Wood & Company, 1933, p 278

19 MacKenna [18]

The continued taking of quinine by mouth or of thiamine hydrochloride by mouth or injection is of clinical and experimental value in the repelling of fleas

Modern insecticides, such as DDT, applied to the known breeding places of fleas offer the most practical solution of the problem

3115 Webster Street (9)

ABSTRACT OF DISCUSSION

DR LESLIE M SMITH, El Paso, Texas I spent the summer of 1925 in the clinic of Dr Harry Alderson at Stanford, and I have had both clinical and personal experience with the hardy California fleas I have seen reactions to their bite so severe and extensive as to suggest erythema multiforme or urticaria That allergy to the toxins injected by fleas and other insects occurs in some persons there can be little doubt This is evidenced by the extreme local reactions which occur in some victims and, I believe, by the appearance of some urticarial lesions which do not occur at the sites of bites, or at least do not contain the puncta of typical bites

In the El Paso area, on account of the very low humidity, fleas are no problem There are mites, bedbugs, mosquitoes and some other insects, and manifestations of allergy are occasionally observed following the bites of some of these In addition to typical bites one occasionally sees scattered urticaria papules, which do not appear to be the result of bites and presumably are an allergic response to absorption of toxin from the bitten areas

I am not prepared to state that in patients encountered in my practice insect bites are the principal cause of lichen-urticatus-like eruptions, but I think it is quite probable that I have not been sufficiently alert to the possibility of this factor in such cases It is a common observation that most cases of lichen urticatus and prurigo occur among the type of patients in whom malnutrition is common These same patients usually live under conditions which favor the presence of insects and the possibility of insect bites I, for one, shall be more conscious hereafter of the possible role of insects in the lichenoid and urticarial papular eruptions

I have had no experience with treatment by desensitization to insect toxins, but the fact that a person may gain tolerance after being repeatedly bitten would seem to indicate that tolerance might be produced artificially by hypodermic injections of the proper antigen I believe this line of reasoning is worthy of further work

In areas where fleas constitute such a problem as they do in California, it is probably wise to give orally or parenterally administered repellents, such as quinine or thiamine, to susceptible persons, but where fleas and other insects are not so numerous I believe the intelligent use of repellent sprays about their breeding places and about the patient's environment will be sufficient for their control

I should like to know what success Dr Lunsford has had with use of the antihistaminic drugs in the control of reactions to insect bites

DR PAUL E BECHET, Elizabeth, N J Dr Lunsford's paper is of interest, in view of the fact that plague-infected fleas (Xenopsylla cheopis) caused the unprecedented death of over 60,000,000 persons from the year 1348 to the end of the Seventeenth Century Another killer of men, typhus, can be carried by fleas as well as by lice, which observation calls attention to the fact that Hieronymus Fracastorius, the author of "Syphilis sive Morbus Gallicus" published "Contagion,

area 80 per cent of the letters had claims that fleas are a real problem Writers from Pasadena, Santa Barbara, Fresno and San Jose disclaimed that there is a flea problem in their localities

The writers described about the same varieties of eruptions as I have described A few specifically mentioned papular urticaria in children

Flea Antigen The great majority of the men stated they had had no experience with the use of flea antigen Most of those who had used it were from California, and their opinions varied from those of its being worthless to others that it was satisfactory in 70 to 80 per cent of cases treated Several men observed that the results were highly successful in some cases and that treatment completely failed in others

Results Reported from the Use of Locally Applied Repellents—The best results reported from the use of locally applied repellents and insecticides were obtained by those persons who used 0 5 to 10 per cent DDT (2,2-bis[*p*-chlorophenyl] 1,1,1-trichloroethane) Many military observers felt that Army 612 (2-ethyl-hexanediol-1,3) is, on the whole satisfactory Others reported varying results from the use of pyrethrum, rotenone and sulfur powder

Reports on the Use of Thiamine Hydrochloride Many of the men had used thiamine hydrochloride given by mouth as a repellent with varied results Eder[20] reported good results in both prevention and treatment Two reports from San Francisco had observations that thiamine hydrochloride administered internally was a 100 per cent effective repellent of fleas in human beings, cats and dogs According to others, it was of questionable value or completely worthless

Selectivity of Fleas Several of the men called attention to the selectivity of the action of fleas That is, very often in a family fleas will bite one member and not another, children being the most frequent victims Those in our office agree that this observation is an accurate one

Some of the men were attacked by human fleas but not by fleas from their own dogs Several observers were attacked by fleas in one geographic location but not in another For instance, fleas in their place of residence in San Francisco did not annoy them, but when they visited Los Angeles or some foreign city, such as Mexico City or Vienna, they would be severely bitten, the reaction in these cases being described as a severe bullous eruption

Some of the men thought that such things as body odor and sex hormones should be considered as accounting for the age and sex selectivity

20 Eder, H L Flea Bites Prevention and Treatment with Thiamin Chloride, Arch Pediat **62** 300 (July) 1945

In our hands, the use of flea antigen has not been convincing in its effects My associates and I have been unable to say that flea antigen has accomplished very much clinically In our hands, the antihistaminic drugs have given some relief

DR. SAMUEL AYRES JR, Los Angeles With reference to humidity, it seems that in our part of the state the flea season is in the hot, dry months, beginning with July, August and September, when the humidity is low The definite instances of flea bites are more pronounced at this time The question of regional immunity is another interesting thing People reaching the Bay area become bitten, and I have also encountered long time residents of San Francisco who have been bitten by our variety of flea One can be immune to California fleas but not to Mexican fleas People may be bitten by cat and dog fleas in any part of the country I know of one person who has been susceptible to dog fleas and is unable to keep dogs Several years ago, in the literature, I ran across an account of an experiment in which a flea was put in the center of a round table and invariably hopped to one person regardless of his position at the table I have had some degree of success with the use of histamine azoprotein (hapamine®) desensitization for highly sensitive persons This drug did not stop the fleas from biting, but the reaction was much less severe An editorial in the *California Medicine* about eight months ago (Hartman, M M *Calif Med* **60** 242, 1947) mentioned the valuable effect of histamine azoprotein in treatment of insect bites Thiamine hydrochloride in a dose of 100 mg three times a day is of definite value in conferring temporary immunity

DR SAMUEL PECK, New York We have had relatively little experience with flea bites in New York city, but, if I may judge on analogy with the investigations which my associates and I carried out during the War ("Cutaneous Reaction Due to the Body Louse," *J A M A* **123** 821 [Nov 27] 1943), it is probable that the flea bite, like the louse bite, is an allergic reaction Pruritus became evident only after allergy was established

Interestingly enough, we could show that the feces as well as the bite of the louse played a role in the cutaneous eruptions which were produced

DR C F LEHMANN, San Antonio, Texas Since the question of allergy is brought up, I rise to testify that I have remained sensitized to the toxin of the flea bites since I was a small boy and was heavily infested with fleas while seeking shelter from a heavy rainstorm one night Ever since then, a flea bite will cause an urticarial reaction not only locally but also generally in me

The diagnosis of such bites sometimes presents quite a problem A child may be brought in with a line of papules with central puncta The flea has the propensity of crawling along a line and biting, and the line of papules is strong corroborative evidence of flea bites, despite the fact that the proud mother might not want to admit such things as fleas having bitten her child These lines of papules are sufficient evidence to substantiate the suspicion of the etiologic factor

DR H S ALDEN, Atlanta, Ga I don't believe that flea bites occur only in California We have them in Georgia In Georgia the "chigger flea" produces most of our troubles I should like to mention the fact that the Negro (the dark Negro, not the mulatto) is more or less immune to the bites of the chigger White men could not be worked in the swamps, but the Negroes could Once I tried to get some students to collect chiggers by laying a sheet or some white material on the ground The chiggers will come to that sheet in large quantities and can be collected I have therefore warned patients never to go into the woods with white shoes or white clothes

DR C J LUNSFORD, Oakland, Calif I thank all the discussers for their expressed interest in my paper

In 1941 McIvor and Cherney [23] treated persons sensitive to flea bites by injecting into them an antigen extracted from whole San Francisco fleas They reported encouraging results

On the basis of data shown in McIvor and Cherney's article the Lilly Research Laboratory prepared an antigen according to the methods developed by the authors but obtained dog, cat and human fleas from Bolivia and Mexico City This extract has been used in our office since it was first manufactured in the treatment of children who were most persistently susceptible to flea bites The results obtained were not controlled and were difficult to evaluate properly because we could not determine whether the "cure" was the result of the injections or was an expression of a natural immunity developed from the patient's being constantly bitten by fleas

Hatoff,[24] using Lilly's commercial antigen and a technic similar to that used by McIvor and Cherney,[23] reported successful desensitization in about four fifths (80 per cent) of children treated

We feel that studies should be made to determine whether or not there is a difference in the antigen injected by fleas of different kinds and from different localities and, if so, of what clinical importance it is

EXPERIMENTS WITH FLEA ANTIGEN

With the cooperation of Drs Bernard H Winston of Kansas City, Mo , and Knox Freytag at the Presidio in San Francisco, together with the residents at Highland–Alameda County Hospital in Oakland, 45 children and 104 adults were tested with the Lilly flea antigen, the tuberculin technic being used Results are so lacking in uniformity that no conclusions can be drawn Therefore, we wish to reserve our findings until they have been rechecked

STUDY OF REACTIONS TO FLEA BITES

It is difficult for one to obtain fleas because of the present day universal use and efficiency of DDT as an exterminator The fleas we have used have been cat fleas, obtained from dogs [25] These fleas were fed on the forearms of volunteers The hungry fleas fed without hesitation When the fleas were satisfied they became active We usually used six to twelve fleas on each subject At times we could get only three or four The fleas will feed three or four times a day and can be kept alive in the test tube with such feedings on the average of only ten to fourteen days

23 McIvor, B C , and Cherney, L S Studies in Insect Bite Desensitization, Am J Trop Med **21** 493 (May) 1941

24 Hatoff, A Desensitization to Insect Bites, J A M A **130** 850 (March 30) 1946

25 The fleas used in our experiments were furnished through the courtesy of Morris A Stewart, Ph D

Clinical Notes

PAIN IN A BREAST DUE TO NEUROSYPHILIS

CARL F BAUMEISTER, M D
RIVERSIDE, ILL
VICTOR P SLEPIKAS, M D
BERWYN, ILL
AND
DUANE D DARLING, M D
CHICAGO

ANY NEW manifestation of syphilis is a matter of clinical interest The literature fails to reveal an authenticated instance of neurosyphilis as a cause of pain in a breast

REPORT OF A CASE

Mrs K D, aged 55, had pain in the right breast, increasing in amount for five years This pain would tend to come in waves of sudden onset, severe intensity and varying duration of one to thirty minutes and would terminate with a feeling of soreness The number of attacks in twenty-four hours would vary, but they were tending to occur almost continuously in the month prior to her hospitalization, which occurred in February 1947 When the patient had an attack and was not taking opiates she could obtain relief only by squeezing her breast violently Since this was not very effectual, codeine or other opiates were given four or five times daily, with partial relief

Since the pain was equally severe and bizarre, the patient had seen numerous physicians, and very complete work-ups, including many serologic tests, had been made Owing to the fact that she could not speak English well and tended to call her bouts "gas pains," her appendix had been removed in 1943 In April 1946, because the gallbladder was poorly visualized, it was removed, the pathologist reported mild fibrosis Neither of these procedures was of the slightest benefit as far as the main symptom was concerned The situation had reached the point that the patient wanted her breast removed

For the last two years she had been having increasing difficulty in vision, tending to have diplopia at times in the last year She had had three normal children, who were all living and well

There were only a few points of pertinent interest in the examination 1 The patient had paresis of the right sixth cranial nerve 2 The reaction to light was sluggish in both eyes but especially in the right 3 The breasts revealed no abnormality 4 Other neurologic findings were not significant

As the patient had had complete gastrointestinal and cardiopulmonary examinations, with roentgenograms and electrocardiograms proving noninformative, it was decided to see if we were not dealing with one of Head's zones of referred pain Accordingly, a lumbar puncture was done for the first time on this patient on Feb 8, 1947, there was no increase in pressure One specimen of spinal fluid examined in the hospital laboratory gave a negative result in the Kahn test, the globulin content was 2 plus, and the Lange colloidal gold curve was 5543221000 A portion of the same specimen sent to the state laboratory gave a positive reaction to the Kahn test, there was no report on globulin, and the colloidal gold curve was 1123322110 As usual, all the serologic tests showed negative results

and twenty-two hours later, fleas were repelled and would not feed on either the subject or 4 other subjects who had not taken thiamine hydrochloride Two days later the fleas fed on the original subject

Four subjects were given 100 mg of the drug intramuscularly at 11 a m, 4 30 p m and 10 30 a m the next day At 1 p m fleas were planted on all subjects and fed for five minutes, and then they quit feeding At 8 a m, 9 a m and 3 p m the next day the fleas would not feed At 8 30 a m the third day most of the fleas were dead The fleas that remained alive fed

Seven test tubes of fleas were fed on 3 subjects given 100 mg of thiamine hydrochloride by mouth, three times a day At the end of six hours the fleas fed reluctantly At subsequent plantings they fed for only five minutes and were inactive At the end of three days most of them were dead

This experiment indicates that at first fleas are repelled but later feed and die when they are planted on patients given thiamine hydrochloride

Fleas were fed on 4 persons with a history of sensitivity to fleas There developed a typical flea bite reaction After the subjects had taken three doses of 100 mg of thiamine hydrochloride, the fleas were again fed on them The subsequent effect was either a less severe reaction or none at all

The question arises as to whether this lowered reactivity was due to the desensitizing or to the repellent action of thiamine hydrochloride

CONTROL OF FLEAS

The most practical method of controlling the flea problem is by means of the newer insecticides, such as DDT If this substance is sprayed onto carpets, floors, overstuffed chairs and basements the fleas will be quickly destroyed It is not necessary for one to apply it to dogs and cats to rid them of fleas Instead it should be sprayed into their kennels or nests or onto their favorite sleeping places One such spraying every two months will keep animals free from fleas

CONCLUSIONS

Flea bites constitute an annoying problem in coastal California, particularly to newcomers in the San Francisco Bay area

My associates' and my experiment of feeding fleas on newborn infants confirms our clinical observations that persons first have to be bitten by fleas in order to become sensitive Our experiments of feeding fleas on old time Californians and on newcomers confirm our clinical findings that most people become immune after having been bitten over long periods

We are certain that most cases of "papular urticaria" in California are, in reality, due to flea bites and suspect that this is probably true elsewhere

Further studies and better antigens are needed for the investigation of the value of artificial desensitization

Oil of citronella, pyrethrum, Army 612, DDT, petrolatum and camphor applied locally are of value as repellents

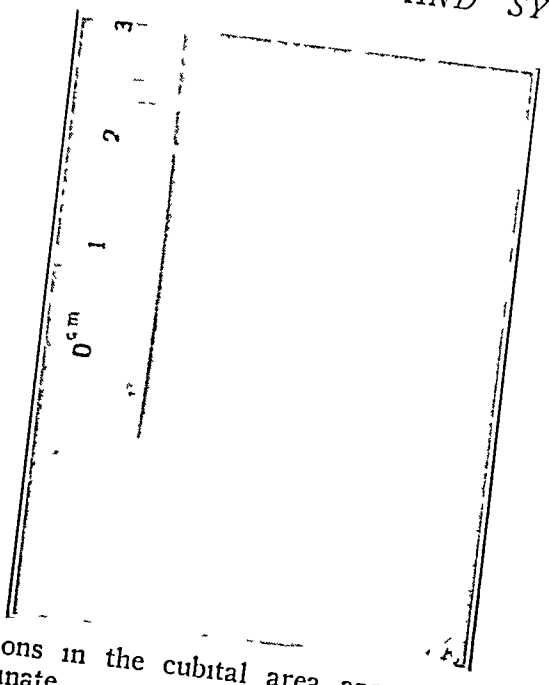


Fig 1—Nodular lesions in the cubital area appearing after an intravenous injection of calcium levulinate



Fig 2—Photomicrograph (× 100) showing foreign body tubercles with giant cells and deposits of calcium

Contagious Diseases and Their Treatment" in 1546, and in his discussion of the etiology of typhus stated that it is caused by a "germinis" transmitted to man by the bite of an insect and not by direct contact or fomites This brilliant observation of Fracastor's four centuries ago was unfortunately completely ignored, had it been acted on and further investigated, it would have saved millions of lives

I hope I may be pardoned for bringing up the lethal importance of the flea, rather than its dermatologic significance, and also that Dr Lunsford may not suffer for his temerity by mentioning fleas and California in the same breath

DR N P ANDERSON, Los Angeles When I first came to California I mistakenly diagnosed flea bites as ordinary urticaria Occasionally the diagnosis of flea bites is made on the findings of bullous lesions the size of a walnut It is hard to conceive that such bullae can be the results of flea bites I think that Dr Lunsford, having access to so many fleas, could disprove the idea that a great many of these lesions are allergic It seems to me that this should be proved or disproved Take these fleas, isolate the person, and let one flea bite him to see whether lesions remote from the bite do occur I don't believe that these so-called remote lesions are allergic I have seen five hundred lesions on one member of my family At certain times of the year there is an epidemic of flea bites Such an epidemic is usually associated with hot spells Endemic cases are seen throughout the year I should also like to mention the transmission of disease by biting insects The bubonic plague first appeared in this country in the Chinese quarter of San Francisco early in the 1900's Oriental fleas carrying the transmittal agent of bubonic plague have been found as far east as Colorado This reservoir of plague extends over the nation and sometime in the future may burst forth into an epidemic

DR NORMAN EPSTEIN, San Francisco I had the pleasure of reading Dr Lunsford's paper at home, and I think he should be complimented on the well planned investigation which he has made Examination of the literature shows a lack of papers on this subject Those of us who practice dermatology in the San Francisco Bay area will concur in the conclusions which Dr Lunsford has drawn There may be some difference of opinion about certain points Dr Anderson has emphasized the role of the flea in transmitting diseases We are all familiar with that Some of us do not realize that bubonic plague, which is transmitted by the flea, still exists in this country There have been 506 cases of bubonic plague in America since 1900 There have been 300 reported from San Francisco, in 268 of which the patient died The last case was reported in 1942, but we cannot be assured that new cases will not develop when least expected Tularemia is spreading from California throughout the country and into Canada by way of fleas transmitted from one rodent to another I agree that a large majority of the cases of papular urticaria in San Francisco are very likely due to flea bites At times the eruption is so severe that some people have to move from San Francisco One of the most remarkable things about the flea is that it will not bite everyone This selectivity on the part of the parasite can hardly be explained on desensitization alone The work of Shannon in regard to thiamine hydrochloride in the repelling of mosquitoes may have a practical bearing in making certain parts of the world more habitable This work was done in 1933 Eder noted that fleas were repelled from children given thiamine hydrochloride Shannon expressed the belief that this action was due to a change in body odor of the person taking the thiamine hydrochloride Perhaps that is the explanation Usually one sees fleas on logs and flea bites on patients who work in warehouses on wooden floors The lesions are occasionally bullous

and continuous salivation Food intake was very difficult Treatment with bismuth sodium triglycollamate was discontinued, and it took about ten days for the symptoms to subside It was then discovered that the patient had dissolved the tablets of the drug on his tongue, as he could not swallow pills Treatment was resumed, without ill effect, with parenteral administration of bismuth subsalicylate

CASE 2—A 55 year old man with syphilitic valvular heart disease was given bismuth sodium triglycollamate in the usual dosage He returned two weeks later with a generalized papulopustular eruption, which cleared within three weeks after treatment with the drug was discontinued Further treatment with bismuth sodium triglycollamate was then tried, at which time the eruption recurred After one month without therapy, treatment was resumed, without further difficulties, with bismuth subsalicylate administered intramuscularly

It seems appropriate to instruct patients not to dissolve bismuth sodium triglycollamate on their tongue, as this procedure undoubtedly predisposes to reactions within the oral cavity

I think the second case is unusual in that a cutaneous eruption occurred in a patient receiving bismuth sodium triglycollamate, while bismuth subsalicylate given parenterally was tolerated well

82 Broadway

PENICILLIN-RESISTANT EARLY SYPHILIS

Report of a Case

LOUIS WEXLER, M D *
AND
ROBERT N BUGG, M D *
NEW YORK

CAPTAIN HERBERT V ADAMS
AND
LIEUTENANT COLONEL ALLEN D SMITH
MEDICAL CORPS, ARMY OF THE UNITED STATES

Since the inauguration of penicillin therapy, resistant early infectious cases have rarely been encountered To our knowledge only 1 such case has been reported [1]

It is the purpose of this paper to present a case of penicillin-resistant early syphilis

REPORT OF A CASE

A 24 year old Negro was admitted to the Dermatology and Syphilology section on Sept 5, 1946 because of a penile lesion of six weeks' duration After appearance of the lesion no treatment had been sought for three weeks At that time the patient had received one intravenous injection of arsphenamine from a private physician, after which treatment the lesion became swollen and painful and did not heal No further treatment was obtained until his entrance to the hospital At admission, dark field examination revealed Treponema pallidum

From the Dermatology and Neurosyphilis Center, Oliver General Hospital, Augusta, Ga

* Formerly Captain, Medical Corps, Army of the United States

1 Tyson, W G Early Syphilis Resistant to Treatment with Penicillin Report of a Case, J Invest Dermat 6 279 (Oct) 1945

In answer to Dr Leslie Smith's question I have not had sufficient experience with the use of the antihistaminic drugs in the control of reactions to flea bites to permit me to discuss the subject

In answer to Dr Bechet's question as to the part blood-sucking insects play in producing the "cutaneous ills of mankind," my observations have in the main been limited to the bites of fleas In those cases in which the allergic reactions are expressed as generalized urticarial or erythema-multiforme-like eruptions, I think there is no doubt but that a rise in temperature would be present

Dr Anderson's idea of planting fleas on persons suspected of being allergic to flea bites and thus demonstrating whether or not such lesions as bullous ones develop far from the sites of the bites is an interesting one My associates and I hope to be able to follow through on it

I was interested in Dr Peck's experiment, proving that in the case of the louse the antigen producing the cutaneous reaction was obtained from the feces as well as from the salivary glands of the louse The group from the Hooper Institute, who did the original work in preparation of the antigen used by Eli Lilly, ground up the whole fleas, including the contents of the intestinal tract, in the production of their antigen In the case of fleas, however, the clinical observation of inflammatory reaction developing about the central punctum would make it appear likely that the flea antigen is in their salivary glands

We were interested to learn that Drs Epstein, Ayres and Lehmann agreed with us that fleas can produce an allergic response

lusterless, pierced the crusts and scutula There was an offensive "mouse" odor to the scalp There were numerous areas of atrophic scarring with alopecia Examination by means of the Wood filter revealed a dull gray fluorescence of about 60 per cent of the hairs of the scalp Of interest was the fact that the involved hairs were fluorescent throughout their length Several of these hairs were pulled for microscopic examination The hairs pulled with some difficulty, though with no pain to the patient Exerting tension on the hair gave one the same impression as pulling a stiff rubber band, i e, the hairs were distinctly tensile

Two finger nails were involved slightly, the process beginning at the distal lateral portion of the nail Microscopic examination of the nail from these areas showed numerous myceliums

Microscopic examination of hairs treated with a 20 per cent solution of potassium hydroxide revealed large spores, many in long chains and others occurring individually In crusts clinging to hairs, hyphae were extremely numerous The spores were seen within the entire length of the hair shaft Also noted within the shaft were numerous air bubbles

A tentative diagnosis of favus was made, and material was sent to Dr E D DeLameter of the Mayo Clinic and to Mr David Mitzkus of the Mycology Laboratory at the Army Area Laboratory, Fort Sam Houston, Texas, for culture Both laboratories reported growth of Achorion schoenleini

The patient has refused roentgen epilation, and treatment has consisted of manual epilation, with the use of a General Electric Purple X® bulb for fluorescence and topical application of an ointment of 20 per cent zinc undecylenate with 5 per cent undecylenic acid (zincundecate [desenex®]) and other fungicidal preparations Most of the improvement noted is apparently due to the correction of the hygienic status of the scalp At this time the infection is still unchecked

A questionnaire was sent to several dermatologists throughout the state Dr Bedford Shelmire of Dallas stated that he had seen 2 cases of favus, which apparently were endemic, within the past twenty years Dr C F Lehmann and Dr J L Pipkin of San Antonio, reported that "the only cases of favus which we have seen were outside San Antonio" All others questioned stated that they had never seen a case of favus in Texas

112 West Seventh St

CONGENITAL DERMOID INCLUSION CYST

Report of a Case

MAURICE J COSTELLO, M D
NEW YORK
WILLIAM F LOVEBURY, M D
COLUMBUS, OHIO
AND
JOHN F DALY, M D
NEW YORK

Dermoid cysts situated on the bridge of the nose are relatively rare, and while seen occasionally by otolaryngologists they have not been brought to the attention of dermatologists

This type of cyst belongs to the group of tumors found about the nose which, according to Luongo,[1] result from the trapping of a portion of the dermis by

1 Luongo, R A Dermoid Cyst of the Nasal Dorsum Arch Otolaryng 17 755-759 (June) 1933

A tentative diagnosis of neurosyphilis was made, and, starting on February 15, an injection of iodobismitol® (a solution of bismuth sodium iodide and sodium iodide in propylene glycol containing saligenin and acetic acid) was given twice weekly on eight occasions Within three weeks the patient noted a definite diminution of the pain in the breast A total of four injections, each of 2 Gm, of tryparsamide U S P, was given weekly, starting March 19 This therapy was discontinued because, though there was almost complete disappearance of the pain, the vision became much poorer The patient had another course of injections of iodobismitol,® followed by four weekly injections of 45 mg of dichlorophenarsine hydrochloride U S P On June 18 spinal fluid obtained by lumbar puncture revealed 3 plus globulin and gave a negative result in the Kahn test and a colloidal gold curve of 0011211000

The patient refused to see an ophthalmologist In June, when an attempt was made to transfer her to a syphilologist nearer her home, treatment was discontinued

CONCLUSION

A case of pain in the breast due to neurosyphilis is presented, which is believed to be the first of its kind recorded in the literature

GRANULOMA CUTIS CALCINOSUM FOLLOWING INJECTION OF CALCIUM LEVULINATE

CHAIM BERLIN, M D
TEL-AVIV, ISRAEL

A peculiar local untoward incident following an intravenous injection of calcium levulinate came to my observation recently At the site of injection a nodular eruption, which took the appearance of granuloma annulare, developed

REPORT OF A CASE

M D, a boy aged 17, was admitted to the hospital in July 1945 because of peritoneal tuberculosis accompanied with ascites He was given roentgen therapy and intravenous injections of calcium levulinate, with much improvement in his condition Once during such an injection he experienced a painful sensation and slight local redness The physician, fearing a subcutaneous infiltration, stopped the injection immediately But no infiltration occurred, and the redness and tenderness subsided within several hours The next day, a papular eruption appeared at the site of injection When the patient was seen by me, six days after the incident, the left cubital area presented a plaque measuring 1 5 by 1 cm, consisting of pinhead-sized to match head-sized, slightly raised, firm, closely aggregated and partly coalesced nodules with smooth surfaces The color was pinkish to yellowish and became lighter on diascopic pressure The lesions were neither pruritic nor painful Most of the nodules were arranged in a horseshoe fashion, and the plaque closely resembled the picture of granuloma annulare (fig 1) No change was observed during the next two weeks The plaque was then totally excised, and the microscopic examination made by Dr Karplus confirmed the tentative diagnosis of deposits of calcium A report on the examination follows

"Corresponding to the nodules distinctly seen on gross observation, there were foreign body granulomas in the form of tubercles with many giant cells of middle size in the deeper layers of the cutis Most of the cells were fibroblasts, and there

From the Department of Dermatology, Hadassah Municipal Hospital

intrusion of the frontonasal plate between the embryonic nasal dermis and mucosa The bridge of the nose, exactly in the midline, is a common location

Most of these growths are discovered before the fifth year of age Secondary infection is common and is followed by sinus formation, with discharge of sebaceous material and pus Occasionally, as with the patient considered here, the presence of hairs calls attention to these congenital anomalies

REPORT OF CASE

A B, a white girl, was first seen by one of us (M J C) when she was 5 years old Her mother gave a history of noticing a small lesion on the bridge of the child's nose when she was 6 months old Since that time the growth had constantly had small black hairs and a thick discharge coming from the opening in the skin There was no family history of similar lesions or other congenital defects

Physical examination revealed a well nourished, well developed, white female child with no abnormalities except a small, match head–sized opening on the bridge of the nose at the junction of the cartilaginous and bony portions, exactly in the midline From this opening thirty to forty black hairs protruded The hairs were midway between lanugo and terminal adult hairs and could be removed easily with moderate traction On gentle pressure a thick, sebaceous material could be expressed There was little pain and no inflammatory reaction around the opening of the sinus

Treatment, which was carried out by Dr John F Daly, consisted in injecting methylene blue into the cyst to facilitate determination of the exact extent of the lesion An elliptical incision was made around the opening of the sinus, and the growth was completely dissected out It was found to mushroom out under the skin and was about pea sized, extending down to the junction of the cartilage and bone of the nose, but it did not involve either Grossly, the lining of the cyst looked like the skin of the scalp or bearded region

Histopathologic examination of the lining of the cyst revealed a normal-appearing epidermis except for a number of vacuolated cells in the basal layer The dermis contained no abnormal cellular elements but did show a large number of hair follicles with their associated sebaceous glands There was no evidence of sweat glands, a finding which has been consistent in previously reported cases

COMMENT

Congenital dermoid inclusion cysts of the bridge of the nose frequently extend down into the nasal septum and necessitate extensive surgery Other methods of therapy, such as electrolysis or destruction with high frequency current or cautery, often result in inadequate removal, recurrences and poor cosmetic results On one occasion, we saw a lesion such as the one described treated as a sebaceous cyst by electrosurgery with a final result of the development of a basal cell epithelioma

SUMMARY

A case of congenital dermoid inclusion cyst of the nasal dorsum is presented An excellent cosmetic result, with no recurrences of the growth, followed treatment

140 East Fifty-Fourth Street (22)

were only a few inflammatory elements Sections stained with hemalum and eosin revealed in the center broad, calcified, collagenous bundles (fig 2) The fundamental color of the tubercle was somewhat bluer than was that of the surrounding tissue A Kossa stain gave wide impregnation of silver in the fibers throughout the tubercle The nolular occurrence of the process indicated an embolic process, that is to say, during the injection calcium reached the skin through small arterioles"

COMMENT

This strange form of calcinosis is certainly extremely rare On the other hand, it is obvious from the history and the histologic observations that the eruption was a consequence of the injection of calcium levulinate However, nothing definite can be said about the mechanism of the eruption The passage of a calcium compound outside the vein usually produces severe, nonspecific, painful infiltration But in this case it must be assumed that even during the puncture particles of calcium succeeded in reaching the skin There they were dispersed, to cause the formation of reactive nodules

SUMMARY

A case of calcinosis of the skin following an intravenous injection of calcium levulinate is reported Around the site of the injection in the cubital fossa an immediate erythema, accompanied with pain, developed This rapidly subsided and was followed by a group of asymptomatic, small, firm, pinkish nodules, which, with their semicircular arrangement, resembled granuloma annulare Histologically, calcified collagenous bundles and foreign body giant cells were found

9 Montefiore

REACTIONS TO BISMUTH SODIUM TRIGLYCOLLAMATE (BISTRIMATE®)

LOTHAR WIRTH, M D
RENSSELAER, N Y

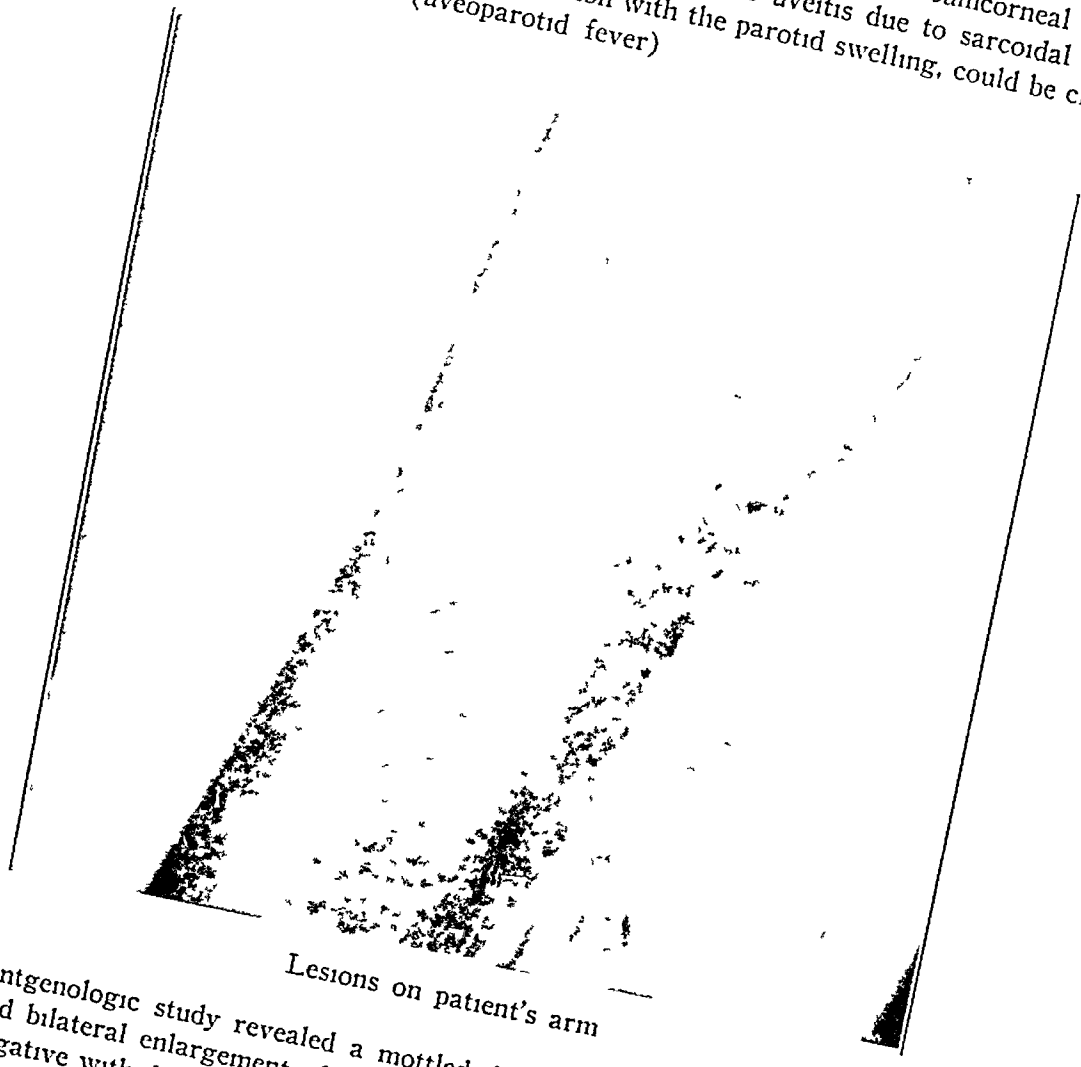
Bismuth sodium triglycollamate (bistrimate®), a new oral bismuth compound for oral administration, has been found effective in systemic bismuth therapy [1] Only minor side reactions, which were limited to the gastrointestinal tract, were observed—reactions which, after dosage had been temporarily reduced, did not interfere with continued administration of bismuth sodium triglycollamate [2] More recently, however, I saw 2 patients exhibit reactions to bismuth sodium triglycollamate which prevented continuation of treatment with this drug, although bismuth subsalicylate given parenterally was tolerated well I thought it might be worth while to report these cases

CASE 1 —A 70 year old man with tertiary syphilis of the central nervous system was started on treatment with bismuth sodium triglycollamate in the recommended dosage of 50 mg three times daily after meals On the third day of this regimen he exhibited an edematous lower lip, bluish discoloration of its mucosa

1 Lehman, R A, and Fassett, D W Experimental and Clinical Studies on Oral Bistrimate (Sodium Bismuth Triglycollamate) for Systemic Bismuth Therapy, Am J Syph, Gonor & Ven Dis **31** 640 (Nov) 1947

2 Gross, E R, and Wright, C S Oral Bismuth Therapy in Syphilis and Various Dermatoses, read before the Pennsylvania Medical Society, Philadelphia, Oct 8, 1946

of subcutaneous hemorrhage on both legs and thighs The oral mucous membranes were dry, and the submaxillary salivary glands were visibly enlarged, firm and of a rubbery consistency The parotid glands were affected similarly, but to a less degree Except for a slight hepatic enlargement and generalized superficial lymphadenopathy, the rest of the general physical examination showed no abnormality Examination with a slit lamp by the ophthalmologic consultant revealed many keratitic precipitates and deposits of pigment on the anterior capsule of the lens of each eye There were numerous clear grayish nodules on the anterior surface of the iris of each eye Moderate circumcorneal injection was present The ophthalomologic diagnosis was uveitis due to sarcoidal involvement, a condition which, in combination with the parotid swelling, could be classified as Heerfordt's disease (uveoparotid fever)



Lesions on patient's arm

Roentgenologic study revealed a mottled density in the lower field of the left lung and bilateral enlargement of the hilar nodes Reactions to the Mantoux test were negative with dilutions of 1 10, 1 500, 1 1,000, 1 10,000 and 1 20,000 History of a positive cutaneous reaction to a tuberculin test four years previously was later obtained from the patient Repeated examinations of sputum, gastric washings and cultures revealed no tubercle bacilli Except for an increase of the sedimentation rate to 47 mm, routine studies of the blood and urine revealed nothing abnormal The plasma globulin level was slightly elevated Serologic tests for syphilis were negative, as was the intracutaneous reaction to Frei antigen (lygranum) Microscopic study of cutaneous biopsy specimens by Dr M R Caro revealed moderate hyperkeratosis of the epidermis, with attenuation of the rete pegs There were focal perivascular accumulations of large mononuclear

and Kahn and Wassermann tests of the blood elicited positive reactions, a diagnosis of primary syphilis was made, and penicillin therapy was started, 100,000 units every three hours for eighty injections During the period that the patient was receiving therapy there was no improvement in the appearance of the chancre On the last day of treatment the prepuce became edematous and nonretractable, and concurrently a generalized, papular, erythematous, discrete, symmetric eruption appeared The papules ranged in size from that of a match head to that of a pea On the next day the eruption was more pronounced and more generalized Dark field examination of one of the papular lesions revealed it to contain living T pallidum, and the titer in the quantitative Kahn test at that time was 20 Kahn units

The patient was then started on a course of oxophenarsine hydrochloride (mapharsen®) and bismuth subsalicylate injections Two weeks later, after the patient had received four injections of oxophenarsine hydrochloride of 0 06 Gm each and two injections of bismuth subsalicylate, 0 2 Gm each, all cutaneous lesions had disappeared, and the titer in the Kahn test was 3 Kahn units At that time the patient was discharged with instructions to report to the local treatment center for completion of therapy, and further contact with the patient was lost

The penicillin used was a crystalline sodium penicillin supplied by the Army and of current stock, the lot number was not recorded at the ward However, concurrent usage in the cases of other patients with primary and secondary stages of syphilis revealed no further deviation from the expected result

SUMMARY AND CONCLUSIONS

A case of penicillin-resistant primary syphilis is presented After having received 8,000,000 units of penicillin, the patient acquired secondary syphilis After this development the response to heavy metal therapy in this case was very favorable

34 West Seventy-Fourth Street

ENDEMIC FAVUS IN TEXAS

BEN R EPPRIGHT, M D
AND
C H McCUISTION, M D
AUSTIN, TEXAS

A white woman aged about 36, consulted us on Nov 3, 1947, because of an eruption of the scalp, with loss of hair

She stated that the disease had begun about one year previously with localized scaliness and mild itching of the scalp The eruption gradually spread, the scaling became severer, and loss of hair ensued in the areas in which the eruption had been present the longest Although born in Poland, the patient had come to Texas twenty-five years ago and had not been out of the state since that time Both the patient and her parents stated that she had had no scalp disease of any kind prior to about a year ago and that no one else in the family had had any disease of the scalp She knows of no contact in the last few years with anyone from foreign countries

Examination revealed a woman of about the stated age, somewhat underweight The entire scalp was involved with scaling and numerous crusts and scutula The scutula were cup shaped, with the concave side facing upward Hairs, dull and

Society Transactions

LOS ANGELES DERMATOLOGICAL SOCIETY

Maximilian E Obermayer, M D, *President*

Franklin I Ball, M D, *Secretary*

Feb 11, 1947

Mycosis Fungoides (with Vertebral Involvement, Treated with Nitrogen Mustard) Presented by DR BEN A NEWMAN

R G, a white woman aged 59, has had a recurrent generalized eczematoid dermatitis for the past eleven years This condition has been treated with several courses of roentgen radiation In 1945 a diagnosis of mycosis fungoides was made from a biopsy specimen During one and one-half years she received roentgen therapy, a course of diphtheria toxoid and injections of antireticular cytotoxic serum without benefit She was admitted to the hospital again on Nov 1, 1946 At that time, she presented a generalized dermatitis involving the entire cutaneous surface, consisting of eczematoid infiltration and plaques

The patient was given two courses of nitrogen mustard (three injections of 6 mg each) during a two week period One week after the first injection, involution of the lesions occurred and also pruritus At the end of three weeks her skin was entirely clear except for a bandlike vesicular patch extending across the right scapula and over the right breast When the vesicular patch became visible, after the generalized dermatitis disappeared, a diagnosis of herpes zoster was made Roentgenologic examination of the spine at this time showed a compression of the fourth dorsal vertebra

The blood cell count, urine and results of the blood chemistry determinations were normal

Mycosis Fungoides (Treated with Nitrogen Mustard) Presented by DR. BEN A NEWMAN

R C, a white woman aged 58, has had recurrent generalized pruritus for thirty years For the past three years, she has been under constant care at the Los Angeles County General Hospital and has been refractory to roentgen irradiation for the past year On Jan 2, 1947, she was admitted to the Cedars of Lebanon Hospital for nitrogen mustard therapy At that time, she presented a generalized eruption consisting of bright red, thick, scaly infiltrated patches

The infiltrate disappeared after three injections of nitrogen mustard, but further therapy was restricted because of a drop in the leukocyte count The pruritus has decreased considerably, and the infiltrated patches are now pinkish and softer

Mycosis Fungoides (Treated with Nitrogen Mustard) Presented by DR BEN A NEWMAN

F S, a white man aged 62, has had a chronic dermatitis of both hands for twelve years Since the beginning, he has had numerous attacks of a generalized eczematoid dermatitis. In each instance, roentgen irradiation was the only agent that produced involution of the eruption, in spite of considerable topical therapy

The present attack began three years ago with generalized eczematoid dermatitis During this period, the patient received repeated courses of low voltage roentgen

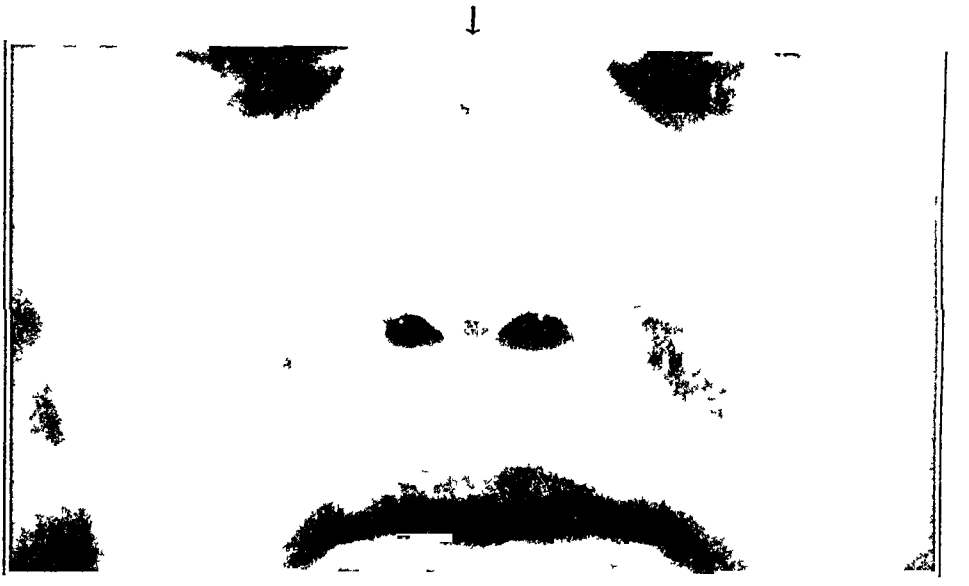


Fig 1—Congenital dermoid inclusion cyst of the nose, with protruding short, black hairs

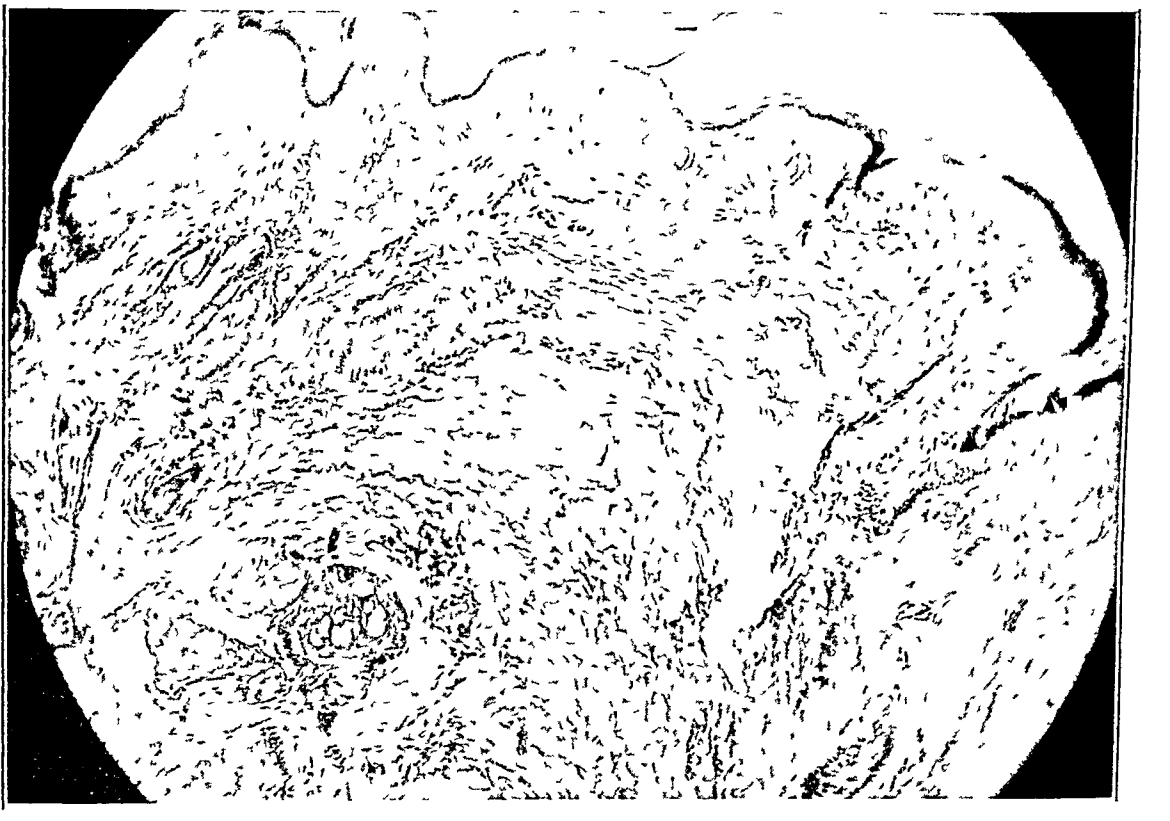


Fig 2—Partial view of the epidermis lining the floor of the cyst, low power magnification, hematoxylin and eosin stain

Nausea and vomiting usually cease after the first two injections The chief contraindication to further therapy is a significant drop in any of the elements of the blood

The patients presented this evening are part of a group of 6 patients with mycosis fungoides receiving treatment and under observation at the Cedars of Lebanon Hospital All the patients were roentgen-ray-resistant, and all have shown a favorable response to nitrogen mustard The degree of response has varied At present, my co-workers and I are studying various dosage and interval schedules of therapy I do not believe that nitrogen mustard will cure this disease, but it has already provided immeasurable relief to some patients With a chemical capable of destroying certain types of neoplastic cells, even temporarily, it is probable that we may be heralding an era of a new method of management (chemotherapeutic) of malignant disease

Darier-Roussy Sarcoid (Gumma?) Presented by DR STANLEY O CHAMBERS and DR STANLEY C ANDERSON

Granuloma Annulare of the Arms and Face. Presented by DR MOLLEURUS COUPERUS

Radiodermatitis with Ulceration (Successfully Treated with Radon Ointment) Presented by DR JUD R SCHOLTZ

Acrosclerosis (Favorable Response of Ulcers to Neostigmine Hydrobromide). Presented by DR MOLLEURUS COUPERUS

DISCUSSION

DR NELSON PAUL ANDERSON I am treating a patient with Reynaud's syndrome and sclerodactylia who has had ulcerations of the finger tips He weighs about 210 pounds (95 Kg) and is 6 feet 2 inches (188 cm) tall We have given him five injections of tetraethylammonium bromide It is apparently a potent drug, because shortly after the injection, which is given very slowly, he can feel increased warmth in the hands and feet and is able to move them with more freedom Just what the ultimate outcome will be, I cannot say, but I do feel that the treatment may at least lead to some useful information It may possibly give an indication as to which are the favorable cases for sympathectomy I doubt that this drug attacks the fundamental perivascular system itself In the October 1946 issue of *Surgery* there is an excellent article on this drug I warn you not to administer the drug when in a hurry, because it is necessary to spend an hour or two with the patient

A Case for Diagnosis (Carcinoma? Pseudoepitheliomatous Hyperplasia Associated with Infectious Mononucleosis and Primary Tuberculous Complex?) Presented by DR J WALTER WILSON

Psoriasis (Hypertrophic Lichen Planus?) Presented by DR NELSON PAUL ANDERSON

A Case for Diagnosis (Lupus Erythematosus?) Presented by DR H C L LINDSAY

LICHEN-SCROFULOSORUM-LIKE LESIONS ASSOCIATED WITH SARCOIDOSIS

Report of a Case

MATTHEW J BRUNNER, M D
AND
MILTON ROBIN, M D
CHICAGO

Lichen scrofulosorum is characteristically associated with a high degree of sensitivity to tuberculin, patients in up to 67 per cent of cases showing positive reactions to old tuberculin in a dilution of 1 1,000,000 [1] The finding of apparently typical lesions of lichen scrofulosorum in a patient exhibiting negative reactions to intracutaneous injections of old tuberculin in dilutions as low as 1 10 is therefore unusual Microscopic examination of cutaneous biopsy specimens in this case revealed a histologic structure characteristic of sarcoid, and on further study laboratory and clinical observations of sarcoidosis involving the eye, salivary glands and lungs were made The association of lichen scrofulosorum with sarcoidosis has been noted on several occasions in cases cited in the transactions of dermatologic society meetings, but the observation of a sarcoidal histologic pattern in lesions of lichen scrofulosorum is apparently unique Mitchell and Nomlund,[2] Cannon,[3] Cornbleet,[4] Michelson [5] and Becker [6] have reported on the clinical concomitance of the two conditions Biopsy of the lichenoid lesions in Cornbleet's case was reported as revealing hematogenous tuberculosis In Cannon's case, the histologic appearance was that of lichen spinulosus

REPORT OF CASE

A mulatto woman, aged 26, was seen in the Department of Dermatology, Research and Educational Hospitals, in August 1946, complaining of joint pains, dryness of the mouth, swelling of the glands of the neck and a cutaneous eruption of three months' duration There had been slight loss of weight, fatigability and low grade fever during this period Examination on admission to the hospital revealed a slender woman, apparently not acutely ill, with an eruption on the neck, shoulders and back, consisting of grouped, acuminate, pinpoint-sized to millet seed–sized, skin-colored papules, some of which were pierced by short, horny spines A few of the patches had cleared centrally to produce annular lesions (figure) There were numerous areas, from the size of a dime to that of a quarter,

From the Department of Dermatology, University of Illinois College of Medicine, Dr F E Senear, Director

1 Sulzberger, M B Dermatologic Allergy, Springfield, Ill, Charles C Thomas, Publisher, 1942, p 234

2 Mitchell, J H, and Nomlund, R Lichenoid Sarcoid and Lichen Scrofulosorum, Arch Dermat & Syph **35** 334 (Feb) 1937

3 Cannon, A B Lichen Scrofulosorum and Sarcoid, Arch Dermat & Syph **38** 91 (July) 1938

4 Cornbleet, T Tuberculosis Cutis (Scrofuloderma, Sarcoid and Lichen Scrofulosorum), Arch Dermat & Syph **38** 272 (Aug) 1938

5 Michelson, H E Sarcoidosis, Arch Dermat & Syph **46** 774 (Nov) 1942

6 Becker, S W Sarcoid (Miliary), Arch Dermat & Syph **48** 223 (Aug) 1943

DR SAMUEL AYRES JR My experience with this disease has been limited to 1 case, and in that instance total destruction was the only method that appeared to be successful—either excision or destruction, with electrodesiccation and curettage I think this is the method of choice

DR NELSON PAUL ANDERSON In Cleveland, at the last meeting of the Academy, Dr Cole showed a patient who had perhaps fifty lesions of porokeratosis of Mibelli around the face and neck Under moderate vitamin A dosage, 25,000 units three times a day, there had been at least a 75 per cent regression, according to the photographs and the condition of the patient Dr Allen in San Diego has a whole family with porokeratosis of Mibelli, with one patient who had ten to twelve lesions on the neck, and there has been dramatic improvement with vitamin A therapy

Chronic Urticaria of Seventeen Years' Duration Presented by DR NELSON PAUL ANDERSON

Tinea Capitis Favosa in a Girl Aged Eleven Years, a Native of the Island of Rhodes Presented by DR M E OBERMAYER and DR J WALTER WILSON

Favus of the Scalp Presented by DR HAROLD E ANDERSON and DR J WALTER WILSON

M K, a white woman aged 28, has had a fungus infection of the scalp continuously since infancy Nine siblings and two paternal aunts are said to have been similarly infected, in some of whom the infection is still present When the patient was 6, the entire family was treated at the Mayo Clinic with roentgen epilation, some were cured This patient states that such epilation was carried out three times in her case Many other attempts have been made at treatment, with uniform lack of success

Examination under Wood's light revealed a dull greenish fluorescence extending along numerous hair shafts for 2 to 3 cm from the scalp Potassium hydroxide preparations of such hairs showed hyphal threads within as well as around the hair shaft, together with chains of spores and occasional air bubbles Culture was obtained on Sabouraud's glucose agar, but only on the third attempt because of secondary involvement with bacterial and nonpathogenic fungi Sufficient growth has been obtained, however, to enable microscopic diagnosis of Trichophyton schoenleini to be made

No treatment has been instituted to date

DISCUSSION OF TWO PRECEDING CASES

DR H P JACOBSON I saw only 1 of the 2 cases The scalp lesions in that patient consisted of several roughly circular patches of inflammatory alopecia with some scarring but no scutula The culture is characteristic The presenter states that topical treatment has proved of no avail My therapeutic suggestion would be topical employment of 15 per cent thymol in oil of thyme The scalp should be shaved once a week, and the thymol application should be put on once daily with an applicator I have had success in the management of tinea capitis (microsporic and trichophytic) with this fungicidal agent

DR. L H WINER The first patient did not have scutula but did have the typical atrophic scars of favus In the second case scutula were present, and on being daubed with alcohol they became yellow, which is a characteristic of favus

cells in the superficial portion of the corium Sharply circumscribed, rounded tubercles were present in the deeper portion of the corium These were composed of syncytial masses of lipid-laden epithelioid cells and a few Langhans' giant cells Lymphocytes were absent, and there were no signs of caseation There were no changes in the epidermis or superficial part of the corium to account for the clinical appearance of follicular papules, although serial sections of two biopsy specimens were studied The pathologic diagnosis was Boeck's sarcoid

Cutaneous lesions persisted unchanged during a two month observation period, which terminated when the patient had an acute schizophrenic episode, which necessitated her transfer to a psychiatric institution

COMMENT

In classifications of cutaneous tuberculosis such as that proposed by Michelson and Laymon,[7] prognosis has been determined by the clinical features of the eruption, and the results of histologic and immunologic studies have been considered of less importance The morphologic aspect of the lesion may, however, prove to be an unreliable index of prognosis On the basis of its clinical appearance, the eruption in the case under discussion was classifiable as a "form which tends to heal relatively rapidly" (lichen scrofulosorum), although laboratory studies, examinations of histologic structure and tuberculin testing suggested a chronic and progressive process Unquestionably, prognosis for the various types of tuberculids depends to a considerable extent on the resistance of the host to the underlying visceral tuberculosis Consideration of all the clinical, bacteriologic, immunologic and histologic findings in any given case is necessary for adequate evaluation of the patient's resistance The relative importance of each of these factors in determining prognosis has not yet been clearly defined, and emphasis on morphology or any other single factor is therefore unjustified In addition, numerous reports attest the fact that lichen scrofulosorum of typical gross and microscopic morphology may occur in conjunction with other tuberculous lesions, i e, lupus vulgaris, which have widely different prognostic significances

SUMMARY

A patient exhibiting lesions clinically typical of lichen scrofulosorum presented histologic and immunologic features of cutaneous sarcoid, as well as sarcoidal involvement of the uveal tract, salivary glands and lungs

Implications relative to the classification of cutaneous tuberculosis are discussed

6230 North Kenmore Avenue (40)

7 Michelson, H E, and Laymon, C W Classification of Tuberculosis of the Skin, Arch Dermat & Syph **52** 108 (Aug) 1945

its growth The dull greenish fluorescence extending for 2 or 3 cm distally along the hair shaft is typical The adult is able to trace the disease through her father to his parents, who came from Luxembourg, the child's parents came from the Island of Rhodes

DR HAROLD E ANDERSON My patient, the adult in the second case, had much heavy, dry scaling extending along and matting together the hair shafts when I first saw her It reminded me of what is called tinea amiantacea A microscopic examination of potassium hydroxide preparation of hairs and scales selected for study revealed numerous mycelia and spores Secondary invaders overgrew the culture mediums, but Dr Wilson was finally able to isolate T schoenleini The familial tendency, the clinical appearance and the cultural study all are typical of tinea favosa She has already had roentgen ray epilation at least three times, once at the Mayo Clinic and once at the University of Iowa She was treated at the Mayo Clinic in 1924 A direct microscopic examination of hairs at that time revealed fungi, but the result of the cultural study was not reported The postepilation therapy was carried out at home in Iowa, and apparently the parents were not diligent enough with this therapy

Basal Cell Epithelioma (Morphea Type) Presented by DR SAMUEL AYRES JR and DR JOSEPH I MIROVICH

DISCUSSION

DR A F HALL In several cases in which I have tried treatment by radiation the condition has proved recalcitrant, I think the lesion has to be destroyed in some other way, such as by cautery

DR ANKER K JENSEN At the risk of repetition, I would again say that in the management of cutaneous malignant growth we must carry out the radical measures first Conservative management is at no time justified in the handling of cutaneous neoplastic disease This applies both to radiation therapy and to surgical procedures I confess partiality to cautery surgery, but of course I am also employing radiation My radiation dosages are much heavier than those employed in the present case I am inclined to agree with Dr Hall that the epithelioma in our present patient has the aspects of a morphea-like lesion, and this could possibly be a factor in its apparent radioresistance There is, of course, little if any danger of distant metastasis from this lesion, it being a basal cell growth The clinical picture at present, however, indicates a steady but progressive extension and activity, and unless eradicated completely it will probably result in a rodent ulcer I recommend radical surgical treatment by means of cautery

DR L H WINER Basal cell carcinomas of the scalp are occasionally of sebaceous gland origin and as such are radioresistant I agree with the preceding discussers that excision followed by skin graft is the treatment method of choice

Blastomycosis of the Foot (North American) Presented by DR W H GOECKERMAN, DR L F X WILHELM and DR MORLEURUS COUPERUS

Acanthosis Nigricans Presented by DR NELSON PAUL ANDERSON

J H D, a white youth aged 18, had a pinkish eruption under the arms, on the sides of the trunk and on the abdomen about three years ago Physical examination at the present time reveals a rough, elevated, dirty brownish reticu-

irradiation with partial relief, but there were prompt recurrences on discontinuance of therapy During the past year, he lost about 15 pounds (7 Kg), chiefly from loss of sleep because of pruritus He was admitted to the hospital on Jan 25, 1947, for nitrogen mustard therapy

Physical examination revealed a generalized eruption consisting of patches and plaques of erythematous eczematoid lesions and erythematous dry infiltrated plaques

On February 3, treatment with nitrogen mustard was started He was given four intravenous injections of 6 mg each in five days On the sixth day, there was visible involution of the lesions and decrease in the itching The patient now presents some residual faint pinkish spots on the legs at the site of the former lesions Histologic examination of the tissue showed the typical polymorphous infiltrate with scattered histiocytes

DISCUSSION OF CASES OF MYCOSIS FUNGOIDES

DR L F X WILHELM I saw a great improvement in the woman who was at the County Hospital for a number of years, but the appearance of her lesions was not altered materially, and when I questioned her about the itching she said that it was still bad I think that we should see these patients again in thirty or sixty days

DR J R SCHOLTZ There appears to be no question that many of the patients treated with nitrogen mustard have been given symptomatic relief and that involution of the skin lesions is substantial Even though there is no assurance of the permanence of the results, the method certainly affords important palliative treatment in a difficult situation

DR A F HALL One patient denied having had any vesicles in the zoster area This zonal eruption appeared in the form of plaques which were themselves suggestive of mycosis fungoides It is of considerable interest to conjecture whether this is herpes zoster If it is, should one assume that it is due to the same virus that produces herpes zoster in otherwise well persons, or is this by any chance a zonal manifestation of mycosis fungoides, or, third, is it just that the eruption takes the form of mycosis fungoides in a person afflicted with that disease?

DR CLEMENT C COUNTER Is the fact that the patient had nausea and vomiting for two days after her injection considered sufficient reason for discontinuing administration of nitrogen mustard, or can it be used again in spite of this reaction?

DR BEN NEWMAN In reply to Dr Hall concerning the zoster-like distribution of the eruption in the first case, this patient had a generalized involvement of the skin with no clear areas except the palms, soles and face One week following a course of nitrogen mustard—methyl-*bis* (β chloroethyl) amine therapy, the entire skin was clear except for the wide patches of lesions that are now present Minute vesicles were scattered among these confluent, erythematous, eczematoid and slightly infiltrated plaques, following the course of the right fourth dorsal nerve The patient had been complaining of radicular pain in this area for two weeks, as well as generalized itching When I became aware of this new lesion, a roentgenogram was taken This showed a destruction of the fourth dorsal vertebra It has been my impression that this patient has a lymphomatous involvement of the vertebra, with radiculitis and herpes zoster, the zoster reaction in a skin already overwhelmed with mycosis fungoides was soon replaced by the lymphomatous response of the skin I believe that this lesion is mycosis fungoides, following a radicular distribution

The patient was then referred to Dr Ralph R Greenson, certified by the American Board of Psychiatry She saw Dr Greenson only three times, at weekly intervals Two weeks after the last consultation, in accordance with a suggestion made during light hypnotic sleep, all verrucae had disappeared

The skin today reveals no trace of the lesions

DISCUSSION

DR A F HALL I think we will all admit that the warts either went away spontaneously or were cured by suggestion, to believe the former demands too much of coincidence I think we will admit that Rasputin, the "black monk of Russia," controlled the czarevitch's hemophilia by suggestion I think most of us, if not all, can cite examples of warts that have been cured by prayer or wishing or out and out suggestion, either in our childhood or in our practice, since Bloch put this type of treatment on a respectable basis, I expect that "suggestion" is the proper word It is intriguing to conjecture regarding the mechanism involved I remember seeing an article on the subject by Karl Zwick in the ARCHIVES (Zwick, K Hygiogenesis of Warts Disappearing Without Topical Medication, *Arch Dermat & Syph* **25** 508 [March] 1932) The author's conjecture is that the treatment of warts by magic and suggestion often includes traumatism of the wart, e g , by rubbing it with a potato or a penny or an apple He also mentions the cure of warts by suggestion without touching the wart He feels that the factor which the two types of approach have in common is perhaps that the wart is unfavorably affected by tissue juices, he advances this theory, because in the inoculation of warts, if any of the innoculum gets into the subcutaneous tissue, a new wart will not appear He further points out that, by psychic methods, extravasation of serum and diapedesis of blood cells can take place under hypnosis He thinks it is through some such mechanism as this that warts may be influenced Were I to "take it from there," I should hypothecate that if there is a tissue fluid or some substance in the corium inimical to warts, it may be the same substance that makes the difference between the bleeding of ordinary tissue and the bleeding of a wart The prolonged bleeding time, seen when a wart is cut, may be due to the absence of thromboplastin in warty tissue, it may be this substance, present in the corium and absent in warts, that is inimical to the "life" of a wart One might try injection of thromboplastin into the base of a wart as treatment, in circumstances which would eliminate the factor of suggestion

DR J R SCHOLTZ In my opinion, most of the treatments that we use for warts act by suggestion, and as far as I am concerned, treatments which are harmless and do not leave scars are the most desirable I can see no therapeutic sense in using any method which causes a scar in place of a benign, harmless lesion There is no doubt that psychotherapeutic methods are effective in the treatment of warts Recently in the clinic of the Los Angeles County Hospital, a boy aged 8 years was seen with four to six large verrucae vulgares on his hands They were bright blue, and it was found that he had been treating them daily with an indelible pencil We encouraged him to continue and stated that the warts would probably disappear in about three weeks On his return a month later, all the warts were gone

DR MAXIMILIAN OBERMAYER There are two reasons for this presentation First, I believe that dermatologists should become better acquainted with the extraordinary fact that an infectious disorder may be amenable to suggestive therapy Obviously, first hand knowledge of the data in an authenticated case

A Case for Diagnosis (Pigmentation of All Finger Tips from Unknown Extraneous Source, Factitious) Presented by Dr J Walter Wilson

A Case for Diagnosis (Dermatitis Vegetans?) Presented by Dr Samuel Ayres Jr

A Case for Diagnosis (Rhinophyma-like Eruption of Face? Lichenoid Eruption of Trunk?) Presented by Dr Samuel Ayres Jr

A Case for Diagnosis (Carcinoma of the Lip? Lupus Erythematosus?). Presented by Dr Thomas W Nisbet

A Case for Diagnosis (Erythema Induratum? Nodular Vasculitis?) Presented by Dr Nelson Paul Anderson

Maximilian Obermayer, M D, *President*

Franklin I Ball, M D, *Secretary*

March 11, 1947

Porokeratosis of Mibelli Presented by Dr Samuel Ayres Jr

N A a white boy aged 12, presents a lesion on the right side of the neck, approximately the size of a nickel with a narrow, elevated border which appears to be made up of individual elements showing dry, hyperkeratotic scaling along the top of the border The lesion developed about nine months ago There is one small pinhead-sized nodule within this circle, and there is a slightly lichenified appearance on the surface of the area enclosed by the ring

Histologic examination reveals that the most characteristic feature is in the epithelial layer, the central portion of which shows hyperkeratosis and parakeratosis with a follicle filled with keratin The prickle cell layer immediately surrounding the follicle is acanthotic, giving the appearance of a ridge with a furrow The basal cell layer is intact, with some perivascular infiltrate in the upper cutis

DISCUSSION

Dr Kenneth L Stout Clinically, I thought this was granuloma annulare, and when I looked at the section I found nothing to change my mind

Dr L H Winer I agree clinically with the diagnosis, but the histologic section did not show porokeratosis of Mibelli Of course, every section of porokeratosis of Mibelli would not necessarily show the characteristic histologic appearance Of interest in the slide are the porokeratotic scales These have been reported adjacent to the hyperkeratotic disks of porokeratosis of Mibelli and are located at the periphery of the disks of porokeratosis However, the infiltration of the cutis was deep and stellate in arrangement I could not see any collagenous necrosis I would suggest another biopsy

Dr Nelson Paul Anderson I think the slide is fairly typical of porokeratosis of Mibelli I think a good deal of variation is seen, depending on (1) the sites of biopsy and (2) where the actual slide is sectioned I happen to have Mibelli's original article on porokeratosis, and I am sure that from a number of photomicrographs in this article one would accept the section as typical

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DR H C L LINDSAY In 1913 Dr Sabouraud showed some patients who had had favus since their earliest days He stated that he had treated the parents of these patients for favus and, furthermore, that in a study of the records of St Louis Hospital, Paris, it was possible to prove that favus had been present in the ancestors of these patients for generations At this time Dr Sabouraud was epilating the scalp of patients with favus with roentgen rays as a preliminary treatment Success in treatment of favus among illiterate persons is most difficult Fortunately, hairs in which favus is growing are not so brittle as when they are invaded by small-spored ringworm Thus favus hairs can be plucked manually Favus was not infrequently seen at St Louis Hospital, and a considerable number of the patients had permanent scars and alopecia in patches

DR CLEMENT E COUNTER Is the temporary epilation of the scalp expected to cure favus? One of these patients presented tonight has had epilation three times She still has the disease

DR BEN NEWMAN In reference to temporary roentgen ray, depilation, our attention should be directed to two important considerations one, that in the past number of weeks approximately a dozen cases of Microsporum audouini infection of the scalp have been uncovered in and around Los Angeles and that we may expect an epidemic form of the disease, if the same pattern is followed here as has occurred in all the larger cities throughout the county, two, that heretofore it has not been necessary, nor has it been the custom, to employ roentgen ray depilation in the treatment of tinea capitis in this area Hence, if we desire to control the spread of this epidemic, we must recognize the need for such depilation and establish this procedure as a proper and customary type of therapy in this community to avoid medicolegal complications Certainly, the merits and need for depilation in Microsporon audouini infections of the scalp require no discussion among dermatologists

DR H C L LINDSAY A few years ago efforts to demonstrate favus fungus in hairs by stain were not always successful Hot carbolfuchsin was used to stain, and dilute nitric acid was used to decolorize Supposedly the decolorizing of the fungi should be slower than that of the other stained material Unfortunately, the hair would decolorize at approximately the same speed Accidentally, I placed some partially decolorized stained hairs containing favus in a watch-glass container which was partially filled with aniline oil I forgot about these hairs for a week When I examined them with the microscope, the fungus in certain parts could be seen retaining the dye, while the rest of the field was clear

DR NELSON PAUL ANDERSON No one has ever seen favus develop in an adult If complete epilation had been carried out on this woman and the disease cured, she would not have been reinfected when an adult Sabouraud said he had never seen a case of favus transferred to an adult I am convinced that certain types of favus are curable by manual epilation I have had 3 cases of favus, 1 involving the thumbnail, 1 involving the scalp of a little girl and 1 involving the scalp of the aunt of the little girl The mother faithfully epilated all the hairs from the scalp of the daughter and faithfully scraped her own thumb nail Both patients are now well The scalp of the maternal aunt still presents widespread involvement

DR J WALTER WILSON I am glad that Dr Obermayer and Dr Anderson afforded me the opportunity of carrying out the mycologic studies in these 2 cases, which I believe are representative of favus under treatment and scrupulous cleanliness Growth of T schoenleini was obtained only with difficulty from the adult because of the presence of other nonpathogenic fungi, which repeatedly suppressed

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lated, papular hyperkeratotic eruption about the center of the trunk, on the anterior and posterior axillary folds and in the pubic region There is also involvement about the inguinal regions and the lower part of the abdomen and in the bends of the elbows The center of the chest and back and the sides of the neck are clear

Histologic examination of the tissue showed a verrucous acanthotic process, with one area where there were four nests of cells just beneath the epidermis, like a nest of melanoma cells Many of the epidermal cells were vacuolated

Treatment has consisted of administration of massive doses of vitamin A, with great improvement The patient has recently been using sodium thiosulfate soaks at the suggestion of Dr E S Lain, of Oklahoma City

DISCUSSION

DR L H WINER My clinical impression was the close resemblance of this case to parapsoriasis, especially in regard to the lesions on the abdomen and flanks However, the verrucous lesions in the right axilla were characteristic clinically of acanthosis nigricans, as was the histologic section Histologically, one cannot differentiate the benign form from the malignant form of acanthosis nigricans

Urticaria Pigmentosa Presented by DR STANLEY O CHAMBERS and DR STANLEY C ANDERSON

Verruca Plana of the Face Treated by Posthypnotic Suggestion Presented by DR MAXIMILIAN E OBERMAYER

D P, an unmarried woman aged 21, noticed the appearance of a group of flat warts on the right side of her chin two years ago The dermatologist who was treating her at that time with fractional doses of roentgen rays for acne vulgaris intimated that the warts would probably disappear with continuation of treatment However, the verrucae spread rapidly, and when the course of roentgen therapy had been completed they involved most of the face Various dermatologists removed the ordinary warts which appeared on the fingers of the right hand by means of electrodesiccation Injections of bismuth subsalicylate in oil, given over a period of eight months, as well as subsequent applications of peeling ointments and solid carbon dioxide and the use of lotions in combination with ultraviolet irradiation, had no effect on the verrucae planae of the face

When I saw the patient for the first time, on Dec 5, 1946, her face was studded with verrucae of the flat juvenile type and lesions were also present on the forehead, the anterior portion of the scalp and the sides of the neck Most of the right side of the face and neck was covered with confluent plaques, while the lesions on the left side were more scattered

When it became clear that the oral administration of bismuth (sobisminol mass) and the local use of a 20 per cent solution of podophyllin in acetone had failed to benefit the patient, her mother was told that I had no other therapeutic suggestions, and the irrational behavior of warts was discussed and illustrated by an account of Dr Bloch's experiments in Zurich A few days after this discussion, the mother suggested that arrangements be made for treatment by posthypnotic suggestion I agreed In order to complete my record of the case, biopsy of a lesion was performed The section showed the features typical of verruca plana juvenilis

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will be much more enlightening than information obtained by hearsay or from an unassimilated skimming of psychiatric literature, as the late Dr Bloch fully realized when he conducted his now famous clinical experiment with Swiss school children Second, I believe that speculation about the nature of the working mechanism underlying the indisputable results of suggestive therapy will prove of value In my opinion, it is most rational to assume that the neurovascular mechanism is involved The psychodynamic factors which lead to contraction of the capillary vessels and consequent pallor in certain emotional states are perfectly familiar Logically one may assume, then, that suggestion can produce a similar spasm of the capillaries, with consequent shutting off of the blood supply to the lesions Dr Greenson approached the problem with such an assumption in mind

Since a preliminary interview revealed no psychoneurotic features, the psychiatrist expressed the belief that while the treatment could produce no ill effects, its chance of success was small At the end of the first interview, the patient was told to imagine for a few minutes before bedtime each night that her face was covered by cold compresses and was beginning to itch and tingle At her second visit, she gave the encouraging report that she had had the sensation of itching An attempt at hypnosis was followed only by a state of deep relaxation without sleep, during which it was suggested that her face would feel cold, her skin would itch and the warts would begin to fall off The patient began the third and last consultation by stating that the warts had commenced to become scaly Once more hypnosis was attempted, and a state of light sleep was produced It was then suggested that her face would feel cold and turn pale and that the lesions would itch and fall off within two weeks The patient was awakened and told that no further interviews were contemplated because her warts would shortly disappear Two weeks later her skin was clear of all lesions

I should be the last to propose that posthypnotic suggestion be employed routinely in the treatment of verrucae On the other hand, since the shortcomings and unreliability of all the so-called approved methods of treating warts are well known, I believe that suggestive therapy should be given a trial when conventional methods have proved useless and extensive involvement has raised a problem from the cosmetic standpoint, as in this case That such therapy will succeed with only a limited number of patients is obvious and that it should be carried out only by a fully trained psychiatrist well versed in the technic and aware of the dangers of hypnotic suggestion is equally clear Certainly most dermatologists would willingly accept a dozen failures with psychotherapy rather than invite a single instance of the dermatitis actinica produced by roentgen therapy The sooner suggestive therapy is given a fair and unbiased trial by the dermatologic profession the sooner its limitations and suitability will be established

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Sullivan M Podophyllotoxin, *1

reactions One patient was transferred to a regimen of aqueous penicillin under hospital supervision and completed his treatment under diphenhydramine hydrochloride (benadryl®) without further difficulty Treatment of the second patient, who had seronegative primary syphilis, was stopped following the fifth injection (3,000,000 units) Further treatment was not given and the patient has maintained seronegativity to date Several Detroit physicians have been using this ambulatory schedule in their practice One relates an interesting experience in which a patient failed to advise the physician immediately as to his reactions He had a severe urticarial reaction following the sixth injection, a much milder reaction following the seventh, a mild reaction following the eighth and none thereafter It is our impression that the incidence of allergic reactions is higher on this regimen than with use of penicillin in peanut oil and wax on a daily injection schedule or with aqueous penicillin This higher incidence could probably be anticipated because of the time between injections and the longer schedule of treatment

TABLE 3.—*Length of Time Required to Complete Course of Treatment*

No of Weeks	No of Cases	Per Cent of Cases
8	40	57 2
9	12	17 2
10	6	6 6
11	4	5 7
12	4	5 7
13	1	1 4
14	1	1 4
15	2	2 8

The accompanying chart is a graphic representation of the cumulative failure rates of various schedules of penicillin therapy used at the Detroit Social Hygiene Clinic between 1944 and 1946 Intensive methods of case holding were not used beyond a year, and many cases were lost from observation

In some instances there is a sharp rise toward the end of the period of observation This rise seems to occur when there are relatively few of the cases remaining under observation A few failures (or possible reinfections) at this point have a pronounced influence on the cumulative failure rate In treatment type F (80,000 units every three hours for one hundred and twenty injections, or 9,600,000 units) the failure rate at eighteen months is 6 1 per cent, while at twenty-four months it is 21 5 per cent Two failures occurred during the last six month period However, only 13 cases were still under observation during that time, which accounted for the 15 4 per cent increase in the cumulative failure rate If all 57 patients treated in this schedule had still been under observation, the failures noted at this time would have increased the cumulative failure rate only 3 5 per cent It seems, therefore, that no

Tinea See also Ringworm
Amiantacea See Seborrhea
Capitis See Ringworm
Favosa See Favus
glabrosa dermatophytosis, onychomycosis pityriasis versicolor, erythrasma and tinea versicolor appearing in same patient 811
sycosis or localized sycosis vulgaris, 127
versicolor, superficial mycoses of veterans survey of 1 000 veterans with service diagnosis of dermatomycosis, *742
versicolor, tinea glabrosa dermatophytosis onychomycosis, pityriasis versicolor and erythrasma appearing in same patient 811
Tobacco, pustular psoriasis, healed after tobacco juice soaks, 896
pustular psoriasis treated with tobacco juice soaks 897
Toe Nails See Nails
Toes See Fingers and Toes
Tolmach J A Lupus vulgaris improved from treatment with calciferol (vitamin D2), 970
Sarcoid with results of Kveim test, 987
Tolman, M M Multiple epidermal cysts of skin 927
Mycosis fungoides in 56 year old woman 929
Necrobiosis lipoidica diabeticorum 947
Telangiectasia essential, limited to calves 930
Tongue, alopecia areata atrophic glossitis or acquired anhidrosis 901
glossitis rhombica mediana of Brocq-Pautrier type, case for diagnosis, 891
glossitis rhomboidea mediana 913
hemangiolymphangioma of 943
leukoplakia of tongue buccal mucosa and lips syphilis, 939
lichen planus and/or lupus erythematosus of lips and tongue, oriental sore of fore arm 848
moniliasis of trichophyton purpureum and monilia infection of hands, feet and nails 822
nonlipid granular cell tumors *765
probable triple symptom complex of Behcet scrotal tongue 864
syphilitic glossitis 1014
Torrey, F A Actinic dermatitis case for diagnosis 1038
Bacteremia case for diagnosis 1031
Basal cell epithelioma morphea-like sclerosing type in nasolabial fold 1053
Hodgkin s disease and cutaneous torulosis 1032
Localized scleroderma 1051
Lymphoblastoma 1029
Mycosis fungoides plaque type 1046
Mycosis fungoides, pruritic infiltrated patches 1046
Poikiloscleroderma with calcinosis 1051
Psoriasiform eruption or lymphoblastoma 1032
Psoriasis or lymphoma 1056
Thymoma 1037, 1045
Thymoma case for diagnosis 1029
Torula experimental studies on treatment of human torulosis *726
Hodgkin s disease and cutaneous torulosis 1032
Traub E F Atopic eczema congenital abnormalities, vascular nevus elephantiasis undescended testes 1016
Behcet s syndrome pemphigus or leukemia cutis 848 1012
Circinate sarcoid 853
Dermatitis factitia of both feet case for diagnosis 1000
Dermatophytosis pustular psoriasis or bacterid 1006
Grassing of fungi, preliminary report *272
Multiple vaccination of face (from barber shop) 1021
Psoriasis toxic eruption secondary to dermatophytosis, blue nevus 1012
Purpura hemorrhagica 853
Scleroderma generalized 1012
Tuberculosis case for diagnosis 1011
Trauma lupus erythematosus of face with possible traumatic or trophic causation 125
Trichophyton generalized dermatomycosis (trichophyton purpureum) associated with hyperkeratosis plamaris et plantaris 445
purpureum and monilia infection of hands feet and nails moniliasis of tongue 822
purpureum dermatophytosis of extremities due to 938
purpureum dermatophytosis resembling psoriasis of leg 1015
violaceum infection of scalp 959
Trichophytosis barbae, 823
Trichotillomania, role of emotion in disorders of skin, *1063
Trombidium use of repellents in clinical dermatology, general principles, *777
Tropical Medicine See under names of tropical diseases, as Leishmaniasis, etc
Tropics, severe form of acne developing in tropics *206
Trunk, multiple areas of superficial atrophy of trunk, macular atrophy (?), 1039
Palmar and plantar keratoses (arsenic?) (keratoderma disseminatum palmaris et plantaris)? superficial epithelioma, trunk ulceration, left small toe and left palm (squamous cell epithelioma?), case for diagnosis, 913
rhinophyma-like eruption of face or lichenoid eruption of trunk, 1218
Tubercle Bacilli See Tuberculosis
Tuberculids micropapular, 447
multiple, lichen scrofulosorum now present, 448
necrobiosis lipoidica or tuberculoderm, 802 or sarcoid, 951
papulonecrotic, 906
papulonecrotic, and erythema induratum 891
papulonecrotic, or lupus erythematosus 1057
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Tuberculoderm See Tuberculids
Tuberculosis See also Tuberculids and under names of diseases organs and regions as Ankle, Buttocks, Neck Perineum, Sternum, etc
case for diagnosis, 1011
colliquativa, sinuses, nodules and ulcers of buttock, tuberculosis colliquativa, or actinomycosis, 937
cutaneous, drug eruption or neurotic excoriations 902
cutis, case for diagnosis, 908
cutis colliquativa improved by calciferol therapy 853
cutis (lupus vulgaris), favorable response to therapy with vitamin D, 1039
cutis of buttock or syphilis, 1027
cutis with papulonecrotic sarcoid-like and colliquative lesions, 856
luposa 946 948
luposa cutaneous horn 946
luposa or lupus erythematosus 930
miliaris disseminata faciei 447, 928
of skin, 827
pulmonary moderately advanced lymphangiectasis of vulva secondary to probable tuberculous salpingitis 910
scrofuloderma, Pott s disease and retrosternal abscess 884
tuberculous (?) infection of buttocks and perianal region, 463
verrucosa cutis 823 1041
Tulipan L Dermatitis medicamentosa case for diagnosis 452
Multiple tuberculids, lichen scrofulosorum now present 448
Tinea glabrosa dermatophytosis onychomycosis pityriasis versicolor, erythrasma and tinea versicolor appearing in same patient 811
Tumors See also Adenoma Angioblastoma Angioma, Cylindroma, Epithelioma Fibroma Fibrosarcoma, Granuloma, Hemangioma, Histiocytoma, Leiomyoma, Lymphangioma Lymphoblastoma, Lymphocytoma Lymphoma, Melanoma, Myoma, Neuroma, Paraffinoma, Sarcoma, Syringoma Syringocystoma, Thymoma Xanthoma
nonlipid granular cell tumors 765
Twining H L Keratosis palmaris et plantaris (acquired) 461
Pityriasis rubra pilaris 461
Recurrent lupus erythematosus 820
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Ulcers acrosclerosis (favorable response of ulcers to neostigmine hydrobromide) 1217
livedo reticularis with recurrent superficial ulcerations of feet, 815
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Meleney s See Abdomen ulcers
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of leg dermatitis herpetiformis arsenical keratoses and pigmentation 801
on legs with sickle cell anemia 1042

matic reinfections The only way to keep the statistical analysis reliable is by painstaking case holding and careful evaluation of all cases

COMMENT

This schedule using penicillin in peanut oil and wax offers an interesting introduction to similar schedules now in use which employ procaine penicillin G in oil

A larger series (146 patients) has just been completed using the same schedule with procaine penicillin G in oil (600,000 units twice weekly for eight weeks) Like the Romansky formula (penicillin in peanut oil and wax) this preparation maintains satisfactory levels of the drug in the blood for only twenty-four hours It has the advantage over the latter preparation, however, in that it is more easily administered, much better tolerated locally and causes fewer allergic reactions It is too soon to attempt a therapeutic appraisal of this second (procaine) series It is expected that the results will closely parallel those of the series herein reported Both series represent interrupted levels of penicillin in the blood By a combination of the results in both series, a larger group of treated patients will be available for comparison in later studies which employ the ninety-six hour repository type of procaine penicillin with absorption-delaying properties

Micronized penicillin G in oil with 2 per cent aluminum monostearate added as a water repellent is rapidly replacing both penicillin in peanut oil and wax and plain procaine penicillin in oil This preparation maintains therapeutic blood levels for ninety-six hours after injections of 300,000 units (1 cc) [2] If given in doses of 600,000 units twice weekly it is indicated that satisfactory blood levels will be continuously maintained This ninety-six hour type procaine penicillin maintains a continuous but lower level in the blood without the high peak concentration of penicillin in oil and wax or plain procaine penicillin in oil Good results in the past with arsenic therapy (except for intensive arsenotherapy) have been secured with repeated peak levels of short duration The question whether better results will be secured with the same total dosage in the same period by interrupted peak dosages or continuous but lower levels needs investigation It has been assumed that continuous even if lower concentrations such as are secured by ninety-six hour procaine penicllin of the repository type will prove equally effective if not superior We have begun a third series of cases of early syphilis at the Social Hygiene Clinic of the Detroit Department of Health, using the same schedule but employing the preparation which maintains ninety-six hour concentrations in order to secure data on this point

2 Thomas, E W , Lyons, R H , Romansky, M J , Rein, C R , and Kitchen, D K Newer Repository Penicillin Products, J A M A **137** 1517 (Aug 21) 1948

War See Veterans
Warts See Verruca
Wassermann Reaction See under Syphilis
Waterhouse, L M Mycosis fungoides in patient with psoriasis, 854
Wax crayons, allergy to, report of case, 798
Way, S C Circumscribed myxedema of legs, 1044
Tuberculosis verrucosa cutis, 1041
Verrucous lupus erythematosus or nevus verrucosus, 1041
Weber-Christian Disease See Panniculitis
Webster, J R Chronic discoid lupus erythematosus—persistent despite treatment for 34 years 891
Eosinophilic granulomas of skin, *701
Glossitis rhombica mediana of Brocq-Pautrier type, case for diagnosis 891
Mycosis fungoides or psoriasis 892
Secondary syphilis and granuloma inguinale(?) 902
Ulceronodular syphilis of abdomen, 882
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Wexler L Penicillin-resistant early syphilis *1207
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Annular atrophic lichen planus or scleroderma 997
Axillary hidradenitis suppurativa pyoderma cystic acne in girl aged 15 989
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Lymphoblastoma or mycosis fungoides 853
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Neurodermatitis with cataract and asthma 993
Nevus cerebriformis 989
Pachyonychia congenita (keratosis palmaris et plantaris dystrophia unguium and leukoplakia oris) 816
Reticulum cell sarcoma 1014
Rosacea-like tuberculid of Lewandowsky 1000
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Lupus vulgaris, improved with calciferol therapy, 985
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Macular atrophy or lichen planus atrophicus 853
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Sarcoid, solitary lesion on nose 829
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Leukoplakia sublingual (white sponge nevus?) 867
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Kaposi's varicelliform eruption in infant 869
Lupus erythematosus in girl of 17 years 861
Urticaria pigmentosa of recent origin in adult with no mast cells in section 873
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3 Results would indicate that continuous therapeutic levels of the drug in the blood are not necessary for satisfactory results in the treatment of early syphilis

4 Ambulatory schedules of this type offer great advantages to both physician and patient They are particularly adaptable for the newer repository type of procaine penicillin

5 The question whether the prolonged but lower levels of procaine penicillin in the blood will produce as effective results as the higher interrupted peak levels attained with penicillin in oil and wax remains to be decided

6 Problems which arise through the recent developments in newer penicillin preparations of the repository type require further investigation

1553 Woodward Ave

Biostatistical analysis of the results of treatment of a disease that is chronic in nature indicates that the simple percentage of failures does not give a true picture of the success or failure Dr Margaret Merrill [1] has proposed a statistical method of deriving cumulative failure rates This method considers the time factor during observation and the fact that cases will be lost before the outcome of treatment is ascertained It assumes that lost cases will have the same experience of success or failure as those in which patients remain under observation If Merrill's method of computation is used, the cumulative failure rate of this group after twenty-five to thirty months of observation is 11 3 per cent Seventy-three per cent of the patients possible to observe were examined at this time The cumulative failure rate and the percentage of failures in this series correspond closely This is true because there was a high proportion of the cases held for observation throughout the entire period and there were no additional failures after eighteen months

TABLE 2—*Summary of Results of Penicillin Therapy Against Early Syphilis*

	No	Per Cent
Negative	56	83 6
Seroresistant	4	5 9
Failure	7	10 5

One of the weaknesses of the treatment of early syphilis in the past has been the failure to hold cases until treatment was completed. Conversely, an important advantage of present intensive treatment schedules, particularly under hospitalization, has been the fact that the treatment is completed It is expected and feared that if a return is made to ambulatory treatment, especially if prolonged over a period of weeks or months, the treatment will again become ineffective through failure to hold these cases This is especially true of the average clinic patient It was expected in this group that many of the patients would report for treatment with such irregularity that the schedule would not prove satisfactory Case holding has, however, been surprisingly good in this series, and our 7 failures and 4 seroresistant cases cannot be blamed on irregularity of treatment This cooperation might not, however, be secured in future groups because more than average effort was made individually to encourage these patients to continue their treatment on schedule Table 3 summarizes the regularity of treatment

Treatment was discontinued in the 2 patients who were receiving penicillin in oil and wax twice weekly because of rather severe urticarial

1 Merrill, M Determination of Prognosis Figures in Chronic Disease, Paper no 238, Department of Biostatistics, School of Hygiene and Public Health, Johns Hopkins University, 1946

involved in two papers [5] which it is therefore not necessary to resummarize here There seems to us good reason to recognize the existence of an infection-activation mechanism in the inflammatory dermatoses, particularly the pyococcic group in which not a drug but another infection, and particularly a virus infection, acts as the activator or sensitizer In regions in which the virus infections particularly those of the respiratory and gastrointestinal tract, are common and epizootic or even epidemic, they offer an explanation of the incidence and the up and down or refractory course of a number of the inflammatory dermatoses They may be complicated by other manifestations of a sensitized state such as photosensitivity, broadening of the base of food-and-contact sensitivity, hypersensitivity to foreign protein (vaccines) and to metals (nickel), and even fatal terminations in conditions such as lupus erythematosus disseminatus, in which a widespread grave, probably vascular, allergy is perhaps the underlying pathologic process [6]

The purpose of the present paper is to particularize further on the clinical picture of the virus-pyogen sensitivity sequence, largely with the aid of illustrative case reports

THE CLINICAL PICTURE OF THE VIRUS-PYOGEN SEQUENCE

Our attention was first drawn to the fact that relapse in a group of patients with juvenile or adult acne, with appearance of crops of pustules in an otherwise favorably progressing course, came in chronologic clumps Over a decade it became apparent that these crops of reactors appeared in successive years at somewhat the same time of year Two periods were rather clearly identified, the midwinter, or February-March, period and the August-September period In a patient distribution such as ours, the two seasonal waves among patients east of the Alleghenies can be recognized in any series of carefully taken histories The August-September wave, sometimes spoken of as "summer flu," has been particularly easy to recognize because of the return of young persons to school with common cold or influenza followed by relapse after three or fourth months of almost complete freedom from lesions An element of some confusing possibilities is the ragweed season, whose vasomotor rhinitic and also possibly allergic sensitizing influence in predisposing to infection may intermingle with or simulate the August-September epizootic

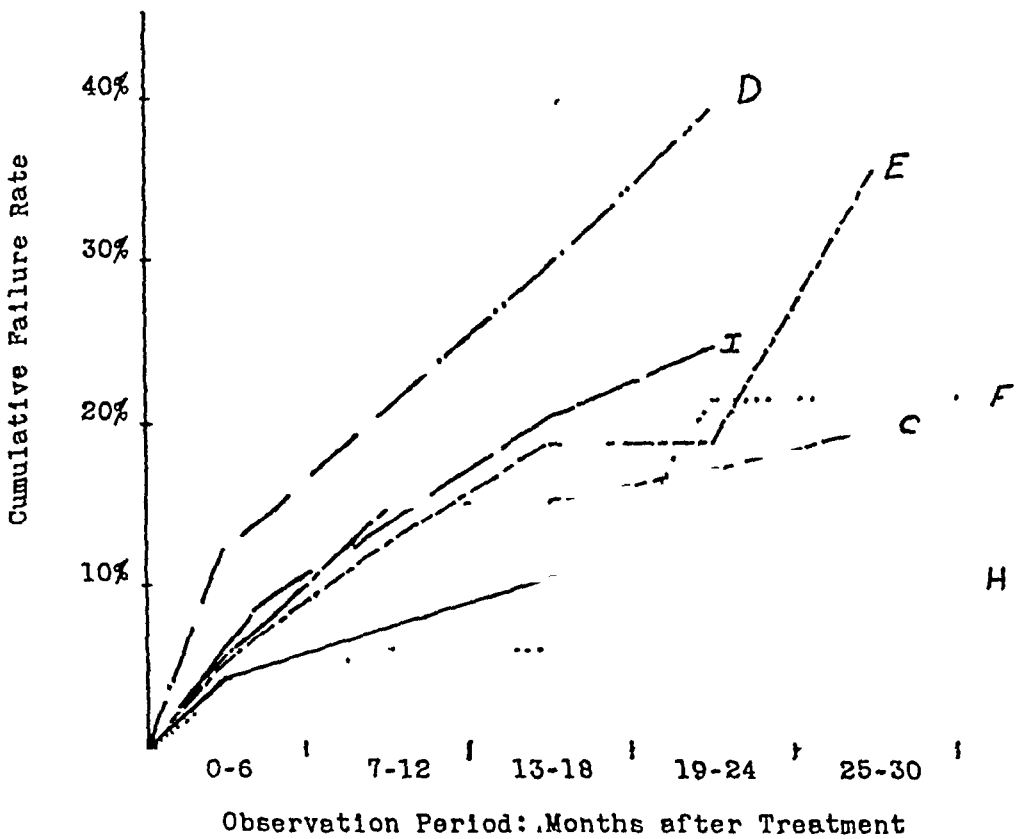
5 Stokes, J H, and Beerman, H Virus Pyogen and Virus Pyogen Photosensitivity Relationships in Cutaneous Disease, Am J M Sc **213** 494-501 (April) 1947 Stokes, J H, and Beerman, H The Dermatology of Yesterday, To-day and To-morrow, in MacKenna, R M B Modern Trends in Dermatology, New York, Paul B Hoeber, Inc, 1948, chap 1

6 Stokes, J H, Beerman, H, and Ingraham, N R, Jr The "Lupus Erythematosus" Concept An Attempt at Integration, Am J M Sc **207** 540-549 (April) 1944

statistical method of analysis will give satisfactory results unless the majority of cases are observed over a prolonged period

Treatment method H, which is described in this paper, shows a relatively satisfactory cumulative failure rate compared to the other methods, and no sharp rise in the failure rate In fact, this comparison shows it to be the most effective of any of the six schedules used The favorable comparsion is influenced by the better than usual case holding (73 per cent) in this group of patients

It is our impression that sharp rises in the failure rate late in the period of observation when many cases have been lost from observation



Cumulative failure rates with various schedules of penicillin therapy treatment methods C, 20,000 units of aqueous penicillin every three hours for 60 injections, 1,200,000 units, D, 20,000 units of aqueous penicillin every three hours for 120 injections, 2,400,000 units, E, 600,000 units of penicillin in oil and wax daily for 8 injections, 4,800,000 units, F, 80,000 units of aqueous penicillin every three hours for 120 injections, 9,600,000 units, H, 600,000 units of penicillin in oil and wax twice a week for eight weeks, 9,600,000 units, and I, 80,000 units of aqueous penicillin every three hours for 60 injections, 4,800,000 units

do not necessarily indicate a high percentage of late failures from the treatment Symptomatic treatment failures, patients with reinfections and those who have had a positive serologic test elsewhere will return to the clinic for advice and treatment Those who consider themselves cured (and may well be cured) do not bother to return We accept the concept that some apparent relapses may be symptomatic or asympto-

6 It is our impression, not as yet statistically studied, that virus infections with pronounced gastrointestinal symptoms (the so-called virus X infections of 1946-1948, for example) are more sensitizing than those of the upper part of the respiratory tract (coryza without sinusitis)

7 The intermingling of virus with pyogenic manifestations is probably more intimate than a precise chronologic sequence would imply For example, outbursts of pyogenic lesions of diffuse character and streptococcic and staphylococcic dermatitis may be synchronous with or even preceded by the appearance of herpes simplex or herpes zoster, and the clinical picture of the Kaposi-like varicelliform eruption may be superposed on or take the place of what at other times in the same eczema-asthma–hay fever patient was a simple crop of scattered staphylococcic pustules

8 A spike or two of high fever from a virus infection at the outset has been seen to improve a staphyloderma, to be followed after the usual week or ten days' refractory period by a pyogenic sensitization flare

9 Sensitization of pyococci probably indigenous to the skin and succeeding bouts of clinical and subclinical virus infection with their associated pyogenic outbreaks are responsible for a good deal of the up and down course and the winter misery of the atropic or eczema-asthma–hay fever group In case 18, after a year of freedom from pyogenic outbreaks at the University of New Mexico, a cold contracted by the patient on the train en route East for the Christmas holiday induced a relapse before the patient reached home

10 One should not be carried away by the virus-pyogen concept to the point of failing to recognize the multiple interacting causes in various types of inflammatory flares, namely, contact and inhalant allergens, emotional crises and photosensitivity The last mentioned, in particular, we have seen exemplified on several occasions

11 Since both a clearcut diagnosis of virus infections and an adequate means of prophylaxis and treatment are lacking, a clinical presentation must remain for the time being somewhat shadowy and impressionistic We have, however, been able to influence the pyogen flare considerably by inducing hyposensitivity to staphylococci with combined vaccine and toxoid therapy using staphylococcus toxoid and bacterial antigen lysed by bacteriophage (ambotoxoid®) Sensitivity to autogenous vaccines has been reported by Norrlind [7]

7 Norrlind, R Prurigo Besnier (Atopic Dermatitis) A Clinical-Experimental Study of Its Pathogenesis with Special Reference to Acute Infections of the Respiratory Tract, Acta dermat-venereol (supp 13) **26** 1-168, 1946

Local tolerance permits large single doses of procaine penicillin Satisfactory blood cencentrations are reported [2] in excess of five days after single injections of 1,200,000 units of ninety-six hour procaine penicillin in oil Weekly injections of 1,200,000 units would be more convenient than two injections of 600,000 units Even if such doses would not maintain therapeutic levels for a full week, our experience with penicillin in peanut oil and wax would indicate that continuous levels are not necessary, it is possible that such single injections might give even superior results Schedules of this type are now being tried out by ourselves and others

The problem of minimum effective dosage and duration of treatment requires more investigation With aqueous penicillin or daily doses of penicillin in oil and wax, 2,400,000 units in eight days seemingly gives as satisfactory results as 4,800,000 units [3] Thomas [4] believes that the duration of treatment is important and that better results are obtained when the same total dose is given in fifteen days rather than in eight days Our observations indicate that treatment with 600,000 units of penicillin in oil and wax twice weekly for eight weeks (9,600,000 units) is effective It is expected that procaine penicillin in oil will prove equally effective The effect of 600,000 units of the latter given twice weekly for four weeks (4,800,000 units) and for only two weeks (2,400,000 units) must be determined Further, the results of single weekly injections of 1,200,000 units of procaine penicillin in oil for two, four and eight weeks must be determined With this information at hand it is possible that more economic schedules permitting better case holding than the eight week schedule herein reported may be employed

SUMMARY

1 Seventy patients with early syphilis were treated with injections of 600,000 units of penicillin G in peanut oil and wax given twice weekly for eight weeks (total 9,600,000 units) They have now been observed for twenty-four to thirty-two months Seventy-three per cent are still under observation The cumulative failure rate has been 11 3 per cent

2 Of the 70 patients, 75 per cent completed the treatment on schedule or within nine weeks, 95 per cent completed their treatment within twelve weeks, and the remaining 5 per cent completed their treatment within fifteen weeks Failures were seemingly not related to irregularity in treatment

3 Heller, J R, Jr , Bowman, R W, and Price, E V Rapid Treatment of Early Syphilis Progress Report December 1947, J Ven Dis Inform **29** 103, 1948

4 Thomas, E W Recent Developments in the Treatment of Syphilis, Am J Pub Health **38** 1361 (Oct) 1948

abated without dermatitic exacerbation on treatment of the patient with castor oil and acetylsalicylic acid Recovery of the child was reported by the mother

Hyposensitization to the staphylococcus and to house dust controlled the recurring virus-pyogen flares

VIRUS EPISODE IN LICHEN PLANUS, PHOTOSENSITIVITY, PENICILLIN SENSITIVITY

CASE 10.—*Diagnostic Summary*.—Typical lichen planus with a virus complication led to sensitivity to light, there was a flare of lichen planus in the light-exposed areas and a flare of previously quiescent dermatophytosis, with possible id, an extension and possible bullous outbreak of the lichen planus occurred, herpes labialis and erythema multiforme (virus type?) developed Possible sensitivity to penicillin with a threatened exfoliative reaction was observed, with eventual recovery

History.—G K, a nervously tense housewife aged 42, presented classic lesions of lichen planus of seven weeks' duration, involving the flexor surfaces of the arms, the thighs, abdomen and soles, with a few typical lesions in the mouth Roentgen therapy, autohemotherapy and calcium therapy, and the intramuscular injection of bismuth subsalicylate resulted in a gradual though fluctuating improvement in five weeks A quiescent dermatophytosis of the feet was suspected but not treated Roentgen radiation was not used on the feet or legs On May 26 a intertrigo of the groin began to appear On June 2 the patient sustained a violent attack of diarrhea due to virus X with abdominal cramps When examined on June 9 she presented (1) a mouth and lips literally filled with lesions of herpes labialis (2) a flare of the previously quiescent dermatophytosis interdigitalis (3) what appeared to be a vesicopustular infection of the id type on the palms (4) a sharp flare of the lichen planus lesions over the flexor surfaces of the forearms, with a sleeve-delineated margin, and diffuse erythema covering the site of exposure to the sun at Coney Island while she had the menses, and (5) almost complete involution of the lichen planus over the covered portion of the trunk and thighs From this point the patient was severely ill with the virus infection and it was feared for a time that a Stevens-Johnson type of erythema multiforme might develop, with profound oral bullous involvement and conjunctivitis The lichen planus increased in extent, a few bullous lesions were suspected among the extending lesions of lichen planus on the trunk A crop of deep papules appeared in the palms, suggesting indurated lichen planus of deep shotty vesicles though fluid was not obtained On the ninth day of septic fever penicillin therapy was begun, however, it was discontinued in forty-eight hours as signs of urticarial edema and slight exfoliation about the eyelids appeared The hands and feet manifested an exfoliative reaction, and the lichen planus gradually subsided When the patient was heard from after discharge, she was steadily improving

The bismuth may have helped to precipitate both the virus outbreak and the dermatologic flare An interplay of drug, virus, photosensitivity and antibiotic was present

VIRUS-PYOGEN SEQUENCE WITH ABDOMINAL MANIFESTATIONS

CASE 12.—*Diagnostic Summary*.—Virus infection of the abdominal type in a pyogen-susceptible child led to, or was accompanied with, appendicitis and terminated in a typical virus-pyogen sequence of pustular lesions, identical with others that had occurred in the past under virus provocation

History.—E A S, a school child aged 9, of allergic parentage, since infancy had been subject to attacks of gastrointestinal and respiratory infection and outbreaks of miliary pustulation in the flexures, over the malar prominences and in the

VIRUS-PYOGEN SEQUENCE

Interrelationship in Inflammatory Dermatoses the Clinical Features

JOHN H STOKES, M D
AND
HERMAN BEERMAN, M D
PHILADELPHIA

IN A SERIES of scattered papers based on observations covering three decades and intensified in the past ten years, Stokes and his associates have outlined a concept of infection allergy which, when applied to the inflammatory dermatoses as an explanation of onsets, relapse and noncure, they have called the virus-pyogen sensitization sequence The effort is comparable to the of Milian [1] in outlining the biotropic concept of the activation of infections by drugs with the production of certain types of so-called drug eruptions To this related field certain observational contributions have been made, particularly in the matter of arsenical exfoliative dermatitis, by Stokes and Cathcart [2] and Stokes and Kulchar [3] Stokes and Callaway [4] pointed out the types of pyogenic relapse that seemed to follow clinical virus infections, including the epizootic seasonal type, often after a lag, or refractory period, of seven to eleven days, following which the sensitization outburst occurred Stokes and Beerman have recently reviewed the literature and done some theorizing on the mechanisms

From the Graduate School of Medicine of the University of Pennsylvania

Read at the Sixty-Ninth Annual Meeting of the American Dermatological Association, Inc, Hot Springs, Va, May 25-28, 1949

This article has been abbreviated in the ARCHIVES by omission of some reports of cases, the complete text will appear in the authors' reprints

1 Milian, G Le biotropisme, Paris, Baillière, Tindall & Cox, 1929

2 Stokes, J H, and Cathcart, E P Contributory Factors in Post-Arsphenamin Dermatitis, with Special Reference to the Influence of Focal and Intercurrent Infection, Arch Dermat & Syph **7**:14-49 (Jan) 1923

3 Stokes, J H, and Kulchar, G V The Infection-Allergic Complex in Arsphenamine Dermatitic Reaction with Special Reference to Dermatophytosis, Brit J Dermat **46** 134-146 (March) 1934

4 Stokes, J H, and Callaway, J L Pyogenic Relapse and Sensitiveness to Light in Certain Dermatoses Influence of a Factor of Intercurrent Infection, Arch Dermat & Syph **36** 976-983 (Nov) 1937

concept Varying with the degree of virus susceptibility and pyogenic susceptibility, we see the clinical picture of virus-pyogen relapse in 1 patient approach the repeated Kaposi varicelliform eruptive type (virus preponderance) while in the person ultrasusceptible to pyogenic responses the relapse after virus infection is, or almost immediately becomes, an impetigo with or without furuncles, a staphylodermic dermatitis or a streptococcic or streptomycotic intertrigo In the fungus-susceptible person with the eczema-asthma–hay fever complex the virus infection seems to emphasize not so much the mycotic as the pyogenic manifestations of the secondary invader

The histaminic mechanism can be drawn into the picture either of the virus or the pyogen-susceptible allergic person or of the subject with an eczema-asthma–hay fever complex by the concept of a shift in intestinal flora toward histamine-producing types[8] (violent supraclavicular and facial flush as in case 12)

In the same way, as indicated in Stokes and Callaway's paper and in several of the foregoing cases, a light sensitization mechanism can be conceived to operate through a shift in intestinal flora, following virus infection, toward porphyrin-producing types or at least types associated with the appearance of porphyrins in stool and urine, whether through hepatic injury or otherwise[4]

Reports of 5 cases are offered as examples of various phases of the virus-pyogen sequence at work among a group of complex causes in the person manifesting eczema-asthma–hay fever susceptibility

CASE 16.—*Diagnostic Summary*.—An extremely pyogen-susceptible person with allergy of the eczema-asthma–hay fever type exhibited multiple causes of relapse after therapeutic response, these demonstrate the instrumentality and the possibilities for confusion of various aspects of the virus-pyogen sequence

History.—W F M, a business man aged 33, had an allergic family background and had been an inveterate pyogen-susceptible person with pyogenic eczema and furunculosis since infancy, complicated by asthma and hay fever and seldom completely cleared In addition he was subject to extreme nervous tension in an exacting and vexatious business, his wife was also a victim of allergic ill health The patient used alcohol in moderation He was only moderately reactive to staphylococcus toxoid and vaccine To multiple inhalant allergens, including pollens, wool, feathers and house dust he was violently reactive He suffered from a self-disclosed Jaquet cutaneous masturbation syndrome with severe excoriation Simply running hot water over the hands of the patient when he was in a paroxysm of itching would produce an ejaculation

In the course of four years' observation this patient was largely cleared once but sustained ups and downs associated with all the aforenamed factors operating

8 Kendall, A I Intestinal Intolerance for Carbohydrate, Associated with Overgrowth of the Gas Bacillus (Bacillus Welchii), J A M A **86** 737-739 (March 13) 1926 Kendall, A I, and Schmitt, F O Physiologic Action of Certain Cultures of the Gas Bacillus Studies in Bacterial Metabolism, J Infect Dis **39** 250-259 (Sept) 1926

Our observation of what we now call the pyogen flare in relation to waves of virus infection then led to additional observations as follows

1 There is a considerable variation in the sensitizing power of different epidemic waves, probably dependent on differences in virus strains or virus type (see subsequent discussion of virus X) There are also differences in persons as to their capacity for sensitization These range from a species of "virus crippling" in which the susceptibility to virus infection is so extreme and the pyogenic flares so severe and invariable that the patient is virtually incapacitated a large part of the time (cases 13 and 17) to instances in which only an occasional virus infection will, over a period of years, give rise to serious relapse

2 To sustain a virus-pyogen flare, it is not necessary for the patient to be sensitized by a severe infection He may have a subclinical infection and flare, or he may have no symptoms of infection while those around him are taken ill A mother may attend her daughter who has influenza and sore throat and, without becoming ill herself, may experience a sharp exacerbation of her dust-contact and atopic eczema A teen-age boy may have a violent flare of his acne but no influenza, while other members of his family fall ill around him

3 The picture of the refractory period as given by Stokes and Callaway (seven to eleven days) is modified by later experience to a range of two to fourteen days from the onset of virus symptoms, probably by the fact that the patient has become a sensitized subclinical carrier before overt symptoms of virus infection appear A patient may have exceedingly slight symptoms (malaise, nasal discharge for a day, two or three loose stools) and be sharply sensitized, while another with fever and prolonged symptoms of sore throat, respiratory difficulty or diarrhea may escape sensitization entirely, even though flaring occurred on some previous or subsequent occasion

4 What appear to be symptoms of virus infection (fever, cramps or gastrointestinal symptoms) may intermingle with or be confused with premenstrual flares and may even occur several times, but there is a tendency for the virus-pyogen flare to occur later, after, rather than before, the period

5 The gastrointestinal symptoms of a significant virus flare-producing infection may range from slight flatulence and constipation, with abdominal cramps for a brief time after the ingestion of food, to a full-fledged attack of acute appendicitis with high fever and enlargement of the mesenteric lymph nodes, with appearance of the characteristic Kaposi-like outbreak a week later as the patient convalesces from the infection plus operation (case 12)

of the Surgeon General of the Army credits Kempe [10] with the demonstration "that the virus infection responsible for the respiratory phase of the diseases lumped together as 'virus X' was influenza virus A, the same flu strain responsible for the epidemic of January, 1947, but quite different from the flu virus of 1943 and 1945." The group of often primary atypical pneumonias associated with erythema multiforme and also the so-called eruptive fever with stomatitis, conjunctivitis and balanitis has been searched for causative organisms, Soll [11] finding little or nothing but suspecting a virus, the Commission on Acute Respiratory Diseases discovering nothing,[12] Finland, Jolliffe and Parker [13] observing some evidence of psittacosis-like virus and a herpes virus, but in only 1 of the last groups' 4 patients was a virus actually recovered from the lung. The role of virus infection in the Kaposi varicelliform eruption has been strengthened by recent reports.

It must be frankly conceded, then, that until the appropriate viruses are isolated, reproduce their symptoms of infection in animals and man, and are followed by pyogenic step-up or invasion, we are still dealing with the suggestive and perhaps presumptive, not the demonstrated, relationship.

It will be recalled that we have noted experiences which make it difficult to hypothesize which comes first, the virus or the pyogenic invasion wave or step-up. Much in point on this matter are Lack's [14] observations on the synergism of some gram-positive cocci and vaccinia virus. Lack found a wave of virus proliferation following a coccic invasion, and he attributed it to the spreading factor, hyaluronidase, produced by the staphylococci. The virus is "spread in proportion to the amount of hyaluronidase produced by a concomitant staphylococcal infection and (2) hyaluronidase-producing staphylococci which produce minimal lesions when injected alone, are spread in proportion to their hyaluronidase production when injected with vaccinia virus." If these observations are confirmed, they suggest an interplay by which, through the mediation of hyaluronidase, a staphylococcus spreads virus and a virus acting to stimulate hyaluronidase production by staphylococci.

10 Release by the Office of the Surgeon General, Department of the Army, Jan. 26, 1948.

11 Soll, S. N.: Eruptive Fever with Involvement of the Respiratory Tract, Conjunctivitis, Stomatitis and Balanitis, Arch. Int. Med. **79**: 475-500 (May) 1947.

12 Association of Pneumonia with Erythema Multiforme Exudativum, Commission on Acute Respiratory Diseases, Arch. Int. Med. **78**: 687-710 (Dec.) 1946.

13 Finland, M., Jolliffe, L. S., and Parker, F., Jr.: Pneumonia and Erythema Multiforme Exudativum, Am. J. Med. **4**: 473-492 (April) 1948.

14 Lack, C. H.: On the Synergism of Some Gram-Positive Cocci and Vaccinia Virus, Brit. J. Exper. Path. **29**: 191-202 (June) 1948.

12 The sensitivity which follows a virus infection tends toward spontaneous remission except in extremely susceptible persons We have seen evidence of spontaneous regression of the pyogenic flare in as little as one week An average duration is from several weeks to three months, judged solely by clinical response

REPORT OF CASES

In the following case histories there are reported a variety of conditions in which the virus-pyogen sequence has been encountered staphylostreptoderma of the ear in association with otic herpes, various infections of hands and feet, acne vulgaris with photosensitivity, dermatophytic pruritus ani, generalized staphyloderma, psoriasis with staphyloderma, generalized psoriasis, lichen planus with photosensitivity, dermatitis herpetiformis, virus X type of infection with abdominal manifestations, and "virus crippling" with repeated pyogenic episodes

VIRUS-PYOGEN EPISODES IN STAPHYLOSTREPTODERMA OF THE EAR

CASE 4.—*Diagnostic Summary*—The virus-pyogen sequence was observed in a patient with staphylogenic and streptogenic dermatitis of the hands and feet She obtained progressive immunity to virus-pyogen flare after prolonged treatment with staphylococcus toxoid and house dust extract

History—K W, a schoolgirl aged 10 was observed two years for intractable dermatitis of the hands and feet Her mother had experienced an identical condition twice The patient had been a feeding problem, with flares on her feet during summers at the shore and on her hands in the fall, the lesions cleared in the winter Following roentgen therapy there was a general follicular, idlike flare In March of the first year of observation, the patient had a severe flare when a cold with fever was treated with sulfathiazole sodium (third dose), and a follicular id developed on her trunk The patient had used a sulfonamide compound locally on a previous occasion without experiencing a bad effect

An abundant local flora of hemolytic streptococci and staphylococci was identified on culture Results of patch testing with shoe, glove and other materials were negative General allergic study revealed decidedly positive responses to glue, stock and autogenous house dust, and some foods There was a slight local reaction but a decided general reaction to staphylococcus toxoid

During the second year of observation this child sustained three virus infections with flares of diminishing severity and a fourth without any cutaneous manifestations The good effect was attributed to simultaneous hyposensitization with house dust extract (autogenous) and staphylococcus toxoid, continued through an entire winter It was noted in one of the virus-pyogen episodes that erythema-multiforme-like lesions appeared on the hands There was some question at one time whether the episodes were not accentuated or even produced by the antigenic toxoid, but the large proportion of injections with this agent did not cause any cutaneous exacerbation Dizziness and epigastric pain had persisted for two days after the last of these toxoid injections, but the symptoms

GASSING OF FUNGI

A Preliminary Report

EUGENE F TRAUB, M D
AND
DANIEL SCHULTHEIS Jr, M D
NEW YORK

THE USE of gas to kill fungi on the skin or scalp has to our knowledge never been tried Gases have been employed to kill bacteria and fungi in fumigating processes in homes and ships and in horticulture In the field of medicine, formaldehyde has been used to destroy myceliums and spores in shoes to prevent reinfection However, the excessively long time of exposure required by this gas plus its irritant action made its use impractical for our purpose The difficulty has been to obtain a relatively harmless gas—that is, one safe to handle, nonlethal to workers and patients and nonirritating to the skin Second, the gas must act in a short enough time to be practical and to kill both the myceliums and spores It was our plan to study various gases to determine whether one could be found which would fulfil our requirements

MATERIAL AND METHODS

The first step was to set up the necessary laboratory apparatus and to establish criteria which would ascertain the fungicidal action of the gases tested It was decided to use subculturing as the basis for determining the fungicidal effectiveness of the gases and also to observe these subcultures for growth for at least two weeks, as was established by Emmons,[1] before a final negative reading was made

For our experiments we used four of the commoner fungi cultured from patients with tinea capitis and dermatophytosis Microsporon audouini, Microsporon lanosum, Trichophyton purpureum and Trichophyton gypseum The fungi were planted on Sabouraud's dextrose agar medium in 300 cc Erlenmeyer flasks, which were stoppered with cotton plugs The cultures were planted with a flamed loop, and the precaution of flaming the mouths of the flasks was also taken to lower the incidence of contamination Only cultures without contaminants were used in our experiments The cultures were allowed to grow out for

1 Emmons, C W Fungicidal Action of Some Common Disinfectants on Two Dermatophytes, Arch Dermat & Syph **28** 15 (July) 1933

creases of the neck The child had no other known allergy and was not sensitive to sulfonamide compounds or penicillin, both of which had been used against repeated attacks of otitis media The individual outbreaks of flexural staphyloderma resolved under local treatment and diminished gradually in severity Even a mild cold had an inguinal intertrigo as a sequel in a week or ten days

In October 1947 the child awakened in the night with violent abdominal pain and rigidity A diagnosis of probable acute appendicitis was made by the pediatrician and the surgeon After exploration an appendectomy was performed the next morning The appendix was inflamed and threatening, but a striking observation was the widespread enlargement and pink color of the mesenteric lymph nodes The leukocyte count before operation did not exceed 13,000 Convalescence was stormy, with high fever and a consistently low leukocyte count Knowledge of the child's history led the dermatologist to predict that by the fifth postoperative day an exanthem of the virus-pyogen sequence type would appear in the flexures and over the malar prominences, this is precisely what occurred The shower of miliary pustules cleared as others had, even without local therapy

A sibling had had repeated attacks of the Peiffer syndrome in childhood, and the family history is criss-crossed with cutaneous and other manifestations of pyogenic infection "allergy"

THE VIRUS-PYOGEN SEQUENCE IN THE ECZEMA-ASTHMA–HAY FEVER (ATOPIC ECZEMA) COMPLEX

The identification and analysis of the part played by virus-type infections in the eczema-asthma–hay fever complex and the atopic and neurodermatitic pictures is made difficult by the multiple interacting causes in these cases In our material, concurrent allergy and the intervention of allergens of all types, but especially the seasonal pollens (ragweed particularly) and the contact-inhalant groups represented in house dust, cause confusion by coincidence in time and by exaggerating respiratory symptoms in which infection may also play a part The person with chronic allergic sinusitis is particularly subject to such puzzling interminglings of symptoms Another group of persons predisposed to the eczema-asthma–hay fever complex is pyogen susceptible, with pronounced familial and personal histories of pyogenic disturbances The xerodermic person with this allergic complex also becomes susceptible when his alkali-neutralizing power is reduced by soap Emotion plays a striking role in the picture of relapse in these patients, and at times the intermingling of emotion and a virus infection (as expressed by a typical herpes and fever with cramps and diarrhea at the height of an emotional storm) is difficult to evaluate In our case material, the instances in which flares of reaction to a locally injected foreign (staphylococcus) protein occur as coincidences suggest something more than emotion as the activator of the pyogenic response The influence of emotion on the nasorespiratory and gastrointestinal shock structures being what it is, their lowering of the threshold of virus and pyogenic susceptibility seems a not unreasonable explanatory

is considerably heavier than air, having an atomic weight of 35 4 and a specific gravity of 2 45 It has been used for many years to bleach cotton and other forms of cellulose and for sterilization Originally it was employed in the form of chloride of lime, or bleaching powder Subsequently it was used as Labarraque's solution, or Javelle solution, which was prepared from chloride of lime by admixture with suitable quantities of alkalis such as sodium carbonate and sodium bicarbonate, and water, the resultant clear liquor was used During World War I chlorine was extensively used in surgical work in the form of diluted sodium hypochlorite solution (modified Dakin's solution) This was a modified and carefully prepared Labarraque's solution with a concentration of about 0 45 per cent sodium hypochlorite In more recent years chlorine has been available as a pure gas compressed in cylinders, and as such has largely replaced chloride of lime

The chemical activity of chlorine in any form used for bleaching or sterilization depends on the exposure of the material to be treated to hypochlorite, which in decomposing to the chloride gives up nascent oxygen

$$Cl_2 + H_2O \rightarrow HOCl + HCl$$
$$2\ HOCl \rightarrow O_2 + 2\ HCl$$

(or as in diluted sodium hypochlorite solution)

$$2\ NaOCl \rightarrow 2\ NaCl + O_2$$

Those who work in plants where bleaching powder and chlorine are manufactured seem to tolerate the gas in high concentrations over long periods of time Diluted sodium hypochlorite solution was used with good results in open infected wounds, where it dissolved and destroyed necrotic tissue and stimulated the formation of healthy granulation tissue Exposure of healthy skin, moist or dry, to chlorine does not seem to result in deleterious effects In testing the gas on our own skin, both moist and dry, only a slight erythema resulted after thirty minutes' exposure to high concentrations

In 1931 Schamberg, Brown and Harkins [2] demonstrated that iodine in 1 85 dilution killed Epidermophyton inguinale after exposure for thirteen minutes Iodine solutions are being used today as fungicides with some good results, especially against dermatophytosis Iodine gas is much too toxic and irritating to be used in our experiments It is mentioned solely because it is a member of the halogen family along with chlorine Attempts were made at this time to increase the activity of iodine by photosynthesis, but the desired effects were not obtained

2 Schamberg, J F , Brown, H , and Harkins, M J Chemotherapy of Ringworm Infection Preliminary Report, Arch Dermat & Syph **24** 1033 (Dec) 1931

singly or in combination Some sensitiveness to sunlight was recognized twice A typical combination of allergic responses is illustrated by flare following a dietary lapse, however, this was preceded by three days of a sneezing episode and fibrositic torticollis There was coincidental exposure to sunlight while the patient was on a fishing trip As another example of the sequence, the patient was free of symptoms in July, August and September (even his ragweed-caused hay fever was delayed a month) At the end of September he sustained a simultaneous attack of allergic rhinitis and diarrhea which persisted for several days, with a simultaneous skin flare The symptoms were relieved almost completely under a regimen of desensitization to house dust and staphylococcus toxoid The skin remained clear for eighteen months On one occasion the patient reacted sharply when injections were given while he had a cold (summation of allergens?) The relapse which terminated this free period had the following causes operative in sequence a visit to the zoo in which he patted sheep (wool allergy), a hunting trip in the latter part of the ragweed season (violent explosion on exposed skin), in December a cold and his wife's influenza led to wholesale extension of the lesions In addition he was subject at this time to intense pressure from business A dose of influenza virus vaccine given to the patient during his wife's illness made his condition sharply worse

A chronic pulmonary or sinus-pulmonary picture began to emerge, and improvement could not be obtained In June the patient had an attack of "erysipelas" with fever, he reported by phone and disappeared from observation

COMMENT AND CONCLUSION

The group of case histories summarized herein is a selection from a much larger number drawn from the files because of long duration of the period of observation and the detail of the history Norrlind helped to validate our anamnestic approach to the virus-pyogen interrelationship in his study of bacterial sensitization in atopic dermatitis, when he found that the overwhelming proportion of the patients who gave self-observed histories of infection flares showed actual bacterial sensitization, while those who did not almost never showed evidence of actual sensitization

In the frequent use throughout this paper of the word virus there is recognition of the inescapable fact that we, and indeed most investigators of so-called virus disease from the clinical side, have failed to find or have not attempted to demonstrate a virus agent in any part of the picture We are proceeding on a clinical assumption that certain recurring groups of symptoms are classifiable as those of virus infection, in part because no other agent can be identified However, the recent literature indicates an increased intensity of search and some positive results in the laboratory in occasional cases Dingle [9] has called attention to the wide diversity of symptoms for which influenza due to Virus A is now accredited A recently released statement by the Office

9 Dingle, J H Common Virus Infections of the Respiratory Tract Diagnosis and Etiology, J A M A **136** 1084-1088 (April 24) 1948

previous epilation of the scalp, because the spores present on the hair shaft within the scalp are not reached by the medicament It is our belief that chlorine can penetrate this barrier and act on the spores there This procedure will be investigated by us as a continuation of this study, as will the effect of chlorine on determatophytosis of the hands and feet

SUMMARY

Four common fungi (M audouini, M lanosum, T purpureum and T gypseum) were exposed in vitro to chlorine After thirty minutes' exposure to this gas it was concluded that the myceliums and spores had been destroyed, inasmuch as the originally gassed cultures and subcultures taken from them showed no signs of life after an observation period of four weeks Chlorine is easily controlled and is relatively non-irritating to the skin Further studies will determine the exact minimum exposure time necessary for in vivo effectiveness against fungi and also whether follow-up or additional treatments will be required

140 East Fifty-Fourth Street

spreads staphylococci However, Lack is careful to say that hyaluronidase is not an exclusive mechanism

We, like other students of the subject, have called the virus-pyogen sequence an allergic or sensitization affair, realizing that we have named but not explained a mechanism Scherago's [15] summary well presents the range of phenomena commonly comprehended by such a term But in saying that a virus infection broadens the base of the allergic state, we have only used another form of words without definition of the mechanism The sensitization studies of Norrlind and of Storck [16] are approaches to a definition of the phenomenon, but they do not yet define its particular mode of activation

Therapeutically, the only suggestions to come from this study of virus activation of other infections, and possibly infection-allergic states specifically pyogenic, perhaps dermatophytic and perhaps miscellaneous (psoriasis and dermatitis herpetiformis) are these A separate use of staphylococcus and bacterial antigen lysed by bacteriophage toxoid (ambotoxoid®), or its combined use with an autogenous house dust extract for hyposensitization purposes showed some signs of reducing the susceptibility of some patients to their virus-pyogen flares A few attempts to hyposensitize with a stock cold vaccine and with autogenous staphylococcus vaccine did not seem promising Climatic escape did not result in a rapid desensitization of the patient from his pyogenic susceptibility, and recurrence followed rather promptly on reexposure to virus

Attention to the other elements of a complex background including other allergens, emotional stress, exhaustion and focal infection remains as important as ever

15 Scherago, M Bacterial Allergy, Ann Allergy **5** 1-18 (Jan.-Feb.) 1947

16 Storck, H Experimentelle Untersuchungen zur Frage der Bedeutung von Mikroben in der Ekzemgenese, Dermatologica **96** 177-262, 1948

epithelioma in the white population of the Southern States supports the concept of an etiologic relationship between solar radiation and skin cancer and emphasizes the importance of the therapeutic problem" [2]

We present herewith certain clinical data on 1,257 additional patients seen from July 1941 through December 1947 with particular attention directed to the histologic observations of 1,025 specimens Dr Kimmelstiel has contributed the histopathologic classification and discussion Since many of these patients have been followed for less than five years, we are not including a tabulation of results in this group It is our intention to supply this tabulation at a later date So far as we can tell at this time, our percentage of cures has not decreased

CLINICAL DATA

In general, the clinical observations made on this group of patients are similar to those published in our previous report, with the exception of those concerning the size of the lesions (table 6) In those tables which include a cross tabulation of one or more clinical findings against the microscopic type of the lesion, we have used the diagnostic terminology employed at the time the specimen was first examined Because Foot's classification of adnexal tumors [3] was not applied to our material until after January 1947, our individual microscopic diagnoses prior to that date were of the generally used standard categories All the 1,025 microscopic specimens, however, have been reviewed and reclassified by Kimmelstiel, his discussion follows the presentation of our clinical data

TABLE 1.—*Age of 1,257 Patients, by Decades*

Decade	Number of Patients	Percentage of Total Number	Percentage Appearing in Previous Report (1,754 Patients)
10 19	5	0 4	0 1
20 29	25	1 9	1 9
30 39	108	8 5	6 9
40 49	236	18 7	15 7
50-59	305	24 2	27 7
60 69	330	26 2	25 3
70-79	205	16 5	18 4
80 89	43	3 4	3 5
90 +	0		

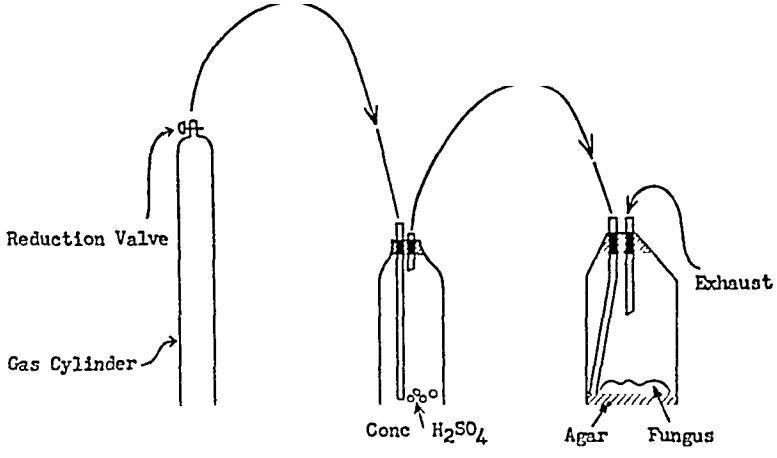
Age.—The age distribution by decades is shown in table 1 The greatest number of cases, 26 2 per cent of the total, occurred in the

2 Elliott, J A, and Welton, D G Epithelioma Report on 1,742 Treated Patients, Arch Dermat & Syph **53** 307 (April) 1946

3 Foot, N C Adnexal Carcinoma of the Skin, Am J Path **23** 1 (Jan) 1947

a period of two weeks and to attain a luxuriant growth before they were exposed to any gas The apparatus used in our experiments is represented diagrammatically in the accompanying figure

The cultures were exposed to several gases for periods ranging from thirty minutes to two hours This was done by slowly running the gas into the bottom of the flask and displacing the air in the flask upward After exposure for the period mentioned, the exposed cultures were subcultured and planted directly on fresh Sabouraud's dextrose agar, again taking the necessary precautions to avoid contamination The subcultures were examined weekly over the period of one month, and the original cultures which had been exposed to the gas were also kept under observation for the same time



Chlorine gas is considerably heavier than air, and by introducing it slowly into the bottom of the flask (40 bubbles per minute) the air in the flask was displaced upward The sulfuric acid bath is for the purpose of further dehydrating the gas

For our experiments, three easily obtainable gases were chosen nitrous oxide, chlorine and carbon monoxide Each of these gases was run through the series of steps previously described Carbon monoxide proved exceedingly difficult to handle and was dropped from the series It certainly would have proved too dangerous for use on a large scale Next, the complete series of steps was run through with nitrous oxide without any remarkable results Exposures up to twelve hours were attempted with this agent, and still there was no evidence of fungicidal action Last, the same procedures were repeated with chlorine (anhydrous) The best results by far in our in vitro experiments were obtained with this gas We repeated the tests several times with chlorine for the exposure times designated, and uniformly excellent results were obtained To date there has been no evidence of growth in cultures of any of the four fungi after thirty minutes' exposure to chlorine

Chlorine is easily handled and controlled Its pungent odor is characteristic, and its yellow-green color is readily recognized The gas

epithelioma, the results here appear at first to be disappointing At least two interfering factors are to be considered, however First, it is difficult, if not impossible, to obtain an accurate estimate of this item from the average patient Second, many of those who are by occupation indoors more than 50 per cent of the time spend an equal or greater amount of time outdoors in various avocations or sustain severe overexposure to sunlight frequently or periodically

Duration We still find this factor difficult to ascertain accurately Although a lesion on the face is usually noticed early by the patient or one of his family, memory of that notation is rarely fixed at a specific date Consequently, a general impression is the best obtainable estimate in most cases Our findings, shown in table 5, are very similar to those reported previously, with the largest number of patients (46 3

TABLE 4.—*Occupational Environment of 1,257 Patients*

	Number of Patients	Percentage	Percentage in Previous Report (1,712 Patients)
Indoor	726	57 5	59 4
Outdoor	535	42 5	40 6

TABLE 5.—*Duration of Epitheliomas in 1,257 Patients*

	Months			Years			
Period *	1 3	4 12	1 3	4 6	7 10	11 20	20+
Number	167	252	582	132	59	47	18
Percentage of total	13 2	20 0	46 3	10 5	4 7	3 7	1 4
Percentage in previous report	14 8	21 6	38 6	13 1	5 8	4 5	1 2

* Period indicates the time between the date the patient recalled having first noticed the lesion and the day he reported for treatment

per cent) waiting from one to three years after noticing a lesion before seeking treatment The frequency increases up to this period of time and decreases uniformly over the longer duration periods With the great amount of cancer education "beamed" at the lay public these days, one may justifiably expect to see the percentage increase in the less than twelve months groups in another five years or so

Size of Lesions The lesions were divided into four groups, according to their surface diameter small (less than 0 5 cm), medium (0 5 to 1 0 cm), large (1 0 to 5 0 cm), and giant (over 5 0 cm) This classification is, at best, only a rough indication, since many epitheliomas are more extensive than their surface appearance indicates Table 6 shows that only 13 5 per cent of all lesions were small, this figure being in decided contrast to that of 45 6 per cent for small lesions in our previous report, the difference may be due to the stressing of

Emmons [3] in 1933 compared the fungicidal action of many agents with phenol and at this time assigned iodine a phenol coefficient of 3,000 against T gypseum and Monilia albicans However, a phenol coefficient was not determined or assigned to chlorine during these studies Still earlier, in 1922, Schamberg and Kolmer [4] determined that mercuric chloride was effective as a fungicide Nowhere in their report was there any mention of the effectiveness of chlorine Of the substances studied, iodine and chlorine (diluted sodium hypochlorite solution) had the highest phenol coefficient by the method used

Bograd [5] in 1943 reported the use of ethyl chloride as a fungicide with excellent results He was unable to find any contraindications to its use, even though in many of the cases reported the lesions became secondarily infected It was his opinion that fungicides in ointment bases definitely retard healing during treatment with ethyl chloride Whether this is also true with regard to chlorine will have to be determined

However, chlorine is not the only gas which is effective as a fungicide Hydrogen cyanide, as reported by Polunin,[6] is effective in killing both colonies and spores of fungi However, this gas is rapidly changed into harmless combinations with the aid of sulfur supplied by compounds of albumin and may, therefore, have little or no effect against fungi when used on human skin Fungi also have a high content of sulfur, which would function in a similar manner and thereby make them more resistant to hydrogen cyanide

It is our belief that chlorine can be used effectively in the treatment of fungous infections of the glabrous skin and scalp Due to its physical characteristics, the gas can be readily controlled The skin will supply the water necessary for the desired chemical reaction, and, as has been shown, this reaction is relatively nonirritating to the skin Chlorine is not suitable for bleaching animal hair for use in textiles because it causes the hair to become brittle and break easily The effect of chlorine on human hair has not been determined as yet, but in treating the scalp it would be desirable to have the scalp clipped or shaved as for roentgenologic epilation To date ointments and solutions used in the treatment of tinea capitis have been relatively ineffective without

3 Emmons, C W Fungicidal Action of Some Common Disinfectants on Two Dermatophytes, Arch Dermat & Syph **28** 15 (July) 1933

4 Schamberg, J F, and Kolmer, J A Studies in the Chemotherapy of Fungus Infections I The Fungistatic and Fungicidal Activity of Various Dyes and Medicaments, Arch Dermat & Syph **6** 746 (Dec) 1922

5 Bograd, N Treatment of Tinea with Ethyl Chloride, Arch Dermat & Syph **48** 511 (Nov) 1943

6 Polunin, N High Concentration Hydrogen Cyanide Fumigation of Fungi and Bacteria, Nature, London **150** 682 (Dec 12) 1942

sexes, but those of the ear were of this type only in men, (5) the distribution by location of the basal-squamous cell lesions was approximately parallel to that of the basal cell lesions (this observation provides

TABLE 7.—*Location and Microscopic Type* of Lesions*

Location (In Order of Incidence)	Male Patients					Female Patients					Grand Total	% of Total No
	B	S	B S	Total	% of Both Sexes	B	S	B S	Total	% of Both Sexes		
Cheek	97	50	9	156	61 1	64	34	1	99	38 9	255	24 8
Nose	97	20	7	124	52 7	79	23	9	111	47 3	235	22 9
Neck	17	19	1	37	56 0	20	4	5	29	44 0	66	6 4
Mucous membrane of lower lip	2	63		65	100 0						65	6 3
Temple	21	12	4	37	58 7	20	5	1	26	41 3	63	6 1
Ear	17	23	2	42	77 7	8	3	1	12	22 3	54	5 2
Nasolabial area (skin of upper lip)	16	1		17	33 3	28	5	1	34	66 6	51	4 9
Forehead	10	6		16	32 0	24	9	1	34	68 0	50	4 8
Body	14	3		17	48 5	8	7	3	18	51 5	35	3 4
Hand	2	19	1	22	66 6	2	8	1	11	33 3	33	3 2
Jaw	11	4	3	18	69 2	4	3	1	8	30 8	26	2 5
Eyelid (skin)	17	2		19	76 0	5	1		6	24 0	25	2 4
Scalp	5	3	1	9	52 9	8			8	47 1	17	1 6
Chin	3	2		5	29 4	9	1	2	12	70 6	17	1 6
Arm	1	1	1	3	27 2	5	3		8	72 8	11	1.0
Finger	2	2		4	50 0	3		1	4	50 0	8	0 7
Leg	1			1	20 0		3	1	4	80 0	5	0 4
Tongue		2		2	40 0		3		3	60 0	5	0 4
Buccal mucous membrane		1		1	50 0		1		1	50 0	2	0 1
Penis		1		1	100 0						1	
Mucous membrane of upper lip							1		1	100 0	1	
Totals	333	234	29	596	58 1	287	114	28	429	41 9	1,025	100 0

* Microscopic type is indicated as follows basal cell epithelioma by B squamous cell, S, and basal squamous cell, B S

TABLE 8.—*Type of Skin and Microscopic Type of Lesion for 1,025 Epitheliomas**

Type of Skin	Male Patients					Female Patients					Grand Total	% of Total
	Number of Lesions				% of Group	Number of Lesions				% of Group		
	B	S	B S	Total		B	S	B S	Total			
Blond	288	203	21	512	85 7	235	106	22	363	84 6	875	84 4
Brunet	45	31	8	84	14 3	52	8	6	66	15 4	150	14 6

* Microscopic type is indicated as follows basal cell epithelioma by B, squamous cell, S and basal squamous cell, B S

an interesting correlation with the histologic classification discussed later in the paper) Sutton presented a similar cross tabulation in his analysis of 560 basal cell carcinomas [4]

4 Sutton, R L, Jr Carcinoma of the Skin, J Missouri M A **39** 203 (July) 1943

EPITHELIOMA

Clinical and Histologic Data on 1,025 Lesions

DAVID G WELTON, M D

JOSEPH A ELLIOTT, M D

AND

PAUL KIMMELSTIEL, M D

Pathologist, Charlotte Memorial Hospital

CHARLOTTE, N C

WHILE the specific etiology of cancer continues to elude detection by any means of investigation known to medical science, epithelium continues to provide both researcher and clinician with an easily available site for studying the behavior of this pathologic mystery The importance of the skin as a site of primary cancer has been recognized apparently since ancient times According to Oberling, "The first primitive notions on what was later to be named cancer must have come from watching *ulcerations of the skin* that were refractory to all treatment, for an account of these in an Egyptian papyrus of the fifteenth century B C constitutes one of the earliest known references to the disease" [1]

Many of our patients, including some of very little formal education, recognize epitheliomas on their own persons and present themselves more or less resigned to what they fear is a serious fate Fortunately, they come in earlier than such patients did years ago, and, with proper treatment, cure is now assured in well over 90 per cent of the cases (with the possible exception of lesions of the mucous membrane)

For some years, two of us (J A E and D G W) have studied the subject of epithelioma with more than ordinary interest Since 1939 we have kept a detailed clinical registry of all the patients with epithelioma whom we have seen In 1941 we reported an analysis of the clinical observations made while we treated 1,742 patients with a total of 1,928 epitheliomas In that report we discussed etiology, the type of skin and the role of pigment, the carcinogenic effect of ultraviolet rays, the prevalence of cutaneous cancer in different areas of the United States and climatologic data Of the 1,052 patients we were able to follow for five years or longer, 97 1 per cent gave every evidence of having been cured We concluded that "the high incidence of

1 Oberling, C The Riddle of Cancer, translated by W H Woglom, New Haven, Yale University Press, 1944, pp 10-15

cell and basal-squamous cell epitheliomas Likewise, in a considerable number of so-called basal cell tumors, tubular-like structures develop in varying degrees of specificity and numbers, making the distinction between basal cell and sudoriparous, hidradenomatous tumors a matter of arbitrary decision

It appeared to us, therefore, that Foot's concept of "adnexal tumor" assists in the understanding of these numerous transitional structures, and we have adopted his classification as a basis for our analysis We attempted in particular to determine how much evidence of differentiation in one or the other direction could be found in so-called basal cell epitheliomas The bulk of the material could be readily fitted into Foot s pattern, but certain exceptions were noted which we believe to be significant and which will be discussed in some detail

The material submitted for histologic study was obtained by curettage In the vast majority of cases the bulk of the tumor and its relationship to the overlying epidermis could be analyzed adequately Five per cent of the specimens had to be discarded as unsatisfactory This method of biopsy of the skin does not permit a survey of the entire mass Variations in the structural pattern of the growth may thus have been missed The resulting inadequacy of accurate classification, however, is believed to have been overcome because of the large number of cases examined and, furthermore, as we concluded, appears to be of little significance

The following table of classification, which is not claimed to approach accuracy, is presented for the purpose of guiding the comment

			Number of Cases	Percentage of Total
I	Squamous cell epithelioma		293	30 3
II	Acanthoma, bordering malignancy		33	3 4
III	Adnexal carcinoma		555	57 2
	A Pilar type			
	1 Pilar type proper	103		
	2 Primordial type	286		
	3 Ribbon type	54		
	4 Cystic type	13		
	5 Unclassified	45		
	B Sudoriparous, glandular type	23		
	C Pilar or sudoriparous type	31		
IV	"Basal celled" type		20	2 1
V	Transitional		67	6 9

CLASSIFICATION OF TUMORS

I *Squamous Cell Epithelioma* We were surprised at the large number of cases in which we were unable to come to a satisfactory conclusion as to whether an acanthotic penetrating epidermis should be called benign or malignant These cases included seborrheic warts and constituted 11 3 per cent of the squamous cell epitheliomas Detailed description is not indicated It suffices to say that we ourselves have

group of patients aged 60 to 69, the next greatest number, 24 2 per cent of the total, were observed in persons in the sixth decade It is clear that the frequency of cutaneous cancer increases with each decade up through the seventh decade, after age 70 there is a relative decline in its occurrence, which observation is explained in great part by the fact that only a small percentage of the population lives beyond 70 years

Sex Of this group of 1,257 patients, 56 4 per cent were men, this figure is 1 per cent less than that reported for men in our previous paper (table 2), in spite of the fact that our present data include reports on lesions of the mucous membrane An analysis of the distribution by sex in the three standard microscopic categories is shown in table 3

TABLE 2—*Distribution by Sex of 1,257 Patients*

Sex	Number	Percentage	Percentage in Previous Report (1,742 Patients)
Male	710	56 4	57 4
Female	547	43 6	42 6

TABLE 3—*Distribution by Sex and Microscopic Type of 1,025 Epitheliomas*

	Cell Type							
	Basal		Squamous		Basal Squamous			Percentage of Total
Sex	Number	Percentage	Number	Percentage	Number	Percentage	Total	
Male	333	53 7	234	67 2	29	50 8	596	58 1
Female	287	46 3	114	32 8	28	49 2	429	41 9
Total	620	100 0	348	100 0	57	100 0	1,025	100 0

We found that the male patients had (1) more than twice as many squamous cell lesions as did the female ones, (2) a majority of the basal cell lesions and (3) virtually the same number of basal-squamous cell lesions as was found in the female patients The only significant sex differential appears in the squamous cell category Although the inclusion of lesions of the mucous membrane in this study undoubtedly contributes to this finding (lesions of the lower lip see table 7), that fact alone is insufficient to account for the entire difference Our findings here are in agreement with those in other reports in the literature which indicate that men are much more susceptible to squamous cell lesions than are women

Occupation In this study we endeavored to ascertain whether or not the occupational environment of each patient was over 50 per cent outdoors, the results are shown in table 4 If one subscribes to the theory that excessive solar radiation is a significant etiologic factor in

factory explanation appears The high percentage of cures of epitheliomas of the skin makes it impossible for us to reevaluate our diagnosis by follow-up of these cases

II *Adnexal Carcinomas*—A Pilar Type Typical examples of all of the subgroups, according to Foot's descriptions and illustrations, could readily be found in relatively large numbers, but the figures given in the tables are far from being accurate, since numerous cases were encountered in which the subgroups were combined in various proportions The degree of differentiation of the "primordial" type into the pilar type proper or ribbon type varies, not only from case to case, but also within various portions of a single section There is, however, no question that the primordial feature is the commonest one We also agree with Foot that whorl formation and keratinization in the center of tumor cell nests are rather common, being characteristic for 22 per cent of all tumors of the pilar type The percentage would have been even higher if we had been strictly consistent and included in this group all cases in which there were isolated or incompletely developed foci of central lamination and formation of squamous-like cells According to description and definition, many of these tumors would appear in other statistics under the term of basal-squamous cell epithelioma

It is questionable to us whether or not the cystic type can be recognized as a separate subdivision The pilar and the ribbon type seem to represent a distinct pattern of differentiation, most of the instances of the cystic type, however, were apparently a result of a degenerative process, the details of which are well known and need not be redescribed Twenty cases of unclassified adnexal tumors are included in which the biopsy specimen was too small for proper subclassification, but sufficiently large to identify nests of the primordial type

B Sudoriparous Glandular Type We have found only 23 tumors for which we are reasonably certain of accurate classification, these growths showing the characteristic features as described by Gates and associates,[6] Foot and others Thirty-one, or approximately 6 per cent, of the adnexal carcinomas showed features which made the distinction between the pilar and the sudoriparous type difficult, and they thus remained open to subjective interpretation Foot admitted this possibility when he stated that lumens in such sudoriparous tumors "may expand into a small cyst, loosely filled with keratinized scales," which is "then difficult to distinguish from an abortive hair" Also there are many cases in which in a primordial type of adnexal tumor there develop cystlike spaces lined by a single or double layer of cuboidal

6 Gates, O , Warren, S , and Warvi, W N Tumors of Sweat Glands, Am J Path **19** 591 (July) 1943

more accurate measurement during the present study The medium-sized lesions accounted for 38 8 per cent, while the greatest number 46 8 per cent was of the large lesions, this observation contrasts strikingly with a finding of 27 9 per cent for this size range in our previous study A few lesions of more than 5 0 cm in surface diameter were classified as giant

Table 6 also reveals the distribution by size among the three standard microscopic types We find that 72 per cent of the small lesions, 62 per cent of those of medium size and 56 per cent of the large lesions were of the basal cell type Thus it is suggested that, the larger the size of the lesions, the higher is the percentage of the squamous cell type

Location That most epitheliomas occur on the exposed portions of the skin is generally recognized In our present study 87 9 per cent of all the lesions occurred on the face and neck, the tabulation for each site is found in table 7 As in our previous report, the cheek and the

TABLE 6—*Size and Microscopic Type of 1,025 Epitheliomas*

Size	Small					Medium					Large					Giant			
Microscopic Type *	B	S	B S	Total	% of Total	B	S	B S	Total	% of Total	B	S	B S	Total	% of Total	B	S	Total	% of Total
Number of lesions	100	32	7	139	13 5	247	127	24	398	38 8	269	185	26	480	46 8	4	4	8	0 7
Percentage of group	72	23	5			62	32	6			56	38	5			50	50		
Percentage of total in previous report					45 6					26 4					27 9				

* B indicates basal cell tumors, S, squamous cell tumors, and B S, basal squamous cell tumors

nose lead as individual sites, accounting for 47 7 per cent of all the lesions These observations represent, in our opinion, important clinical evidence supporting the concept of solar radiation as a significant etiologic agent

Table 7 also presents a detailed tabulation of distribution of lesions according to microscopic type and sex Male patients presented the majority of all the lesions (58 1 per cent) and led numerically in each microscopic type except the basal-squamous cell variety, the occurrence of which was evenly divided numerically (on a percentage basis, the incidence was actually higher in the women) Other significant observations illustrated in this table include the following points (1) All lesions of the lower lip were in men, the one lesion of the mucous membrane of the upper lip, however, was in a woman, (2) male patients presented over two thirds of the lesions occurring on the ear, jaw and hand, (3) women had more than two thirds of the epitheliomas found on the forehead, nasolabial area, chin, arm and leg, and also 60 per cent of the lesions of the tongue, (4) lesions of the hand and of the lower lip were predominantly squamous cell in both

instances again much is left to the imagination of the individual observer Reexamination of these sections at different times often resulted in contradictory conclusions



Fig 3—Transitional type (Different magnifications of the same tumor) *A*, low power view, showing atypical squamous cell growth from the surface, with an adnexal tumor in the depth *B*, medium power view, of a portion of a sudoriparous adnexal type of tumor, with nests of squamous cells indicated by *X*

Type of Skin Another axiom in the lore of cutaneous cancer is that epitheliomas occur much more commonly in blond persons than in brunets While experimental and theoretic considerations cited in our previous report strengthened this general impression, we did not at that time have definite clinical data on this point In our present study we have tabulated data on this factor and found that 84 4 per cent of all the lesions occurred in blonds Table 8 shows this tabulation, also broken down according to microscopic type This information, again, is confirmatory evidence supporting the concept of solar radiation and susceptible skin type in the pathogenesis of epitheliomas

HISTOPATHOLOGY

This histologic analysis is based on a study of 968 specimens [5] previously diagnosed as either squamous cell, basal cell, or basal-squamous cell epitheliomas A large number of these tumors have been shifted vacillatingly from one group into another, and this review was undertaken with an attempt to arrive at a clearer understanding and integration of the various types

A survey of textbooks and current literature leaves the impression that little doubt exists concerning the origin of so-called basal cell tumors from the basal layer of the epidermis or corresponding layer of hair shafts.

In a recent article, however, Foot [3] has given new impetus to Mallory's theory of the "hair matrix carcinoma" He has modified this concept by postulating that these tumors derive from adnexal primordia and accordingly proposed a new terminology and classification He suggested the term "adnexal carcinoma" The justification for this terminology lies largely in the fact that a great number of so-called basal cell tumors show evidence of varying degrees of differentiation, simulating more or less abortive hair follicles, sebaceous glands and sweat glands

In accordance with the accepted principles of oncologic terminology the term basal cell tumor implies that the cells of the tumor maintain the character of basal cells This situation, in our own experience, exists for no more than half the cases The occurrence of squamous epithelial cells, with or without more or less well developed horny pearls, in the center of nests of otherwise typical basal cell epitheliomas is so frequent, the degree of specificity of differentiation so variable and the transition so insidious that inextricable confusion results if one attempts to separate such tumors into distinct entities, such as basal

5 Fifty-seven specimens are not included because the amount of tissue was inadequate to justify a microscopic diagnosis of epithelioma, all these specimens, however, were from clinically epitheliomatous lesions and were therefore included in our clinical tabulations

growth with finger-like projections The buds of "basal" cells not infrequently resemble tubules, and instances have been encountered in which true glandular structures were formed, showing lumens and partial lining by a double row of cells Obvious coil glands, simulating



Fig 4—*A*, low power view of an adnexal carcinoma, pilar type proper, showing features characteristic of epithelioma adenoides cysticum *B*, medium power view of the same tumor

fluctuated in our diagnoses, from one of low grade malignant growth to that of benign growth, on reexamination of these sections Failure to arrive at a definitive conclusion in such a high percentage of cases is not reflected in many other reports, a circumstance for which no satis-

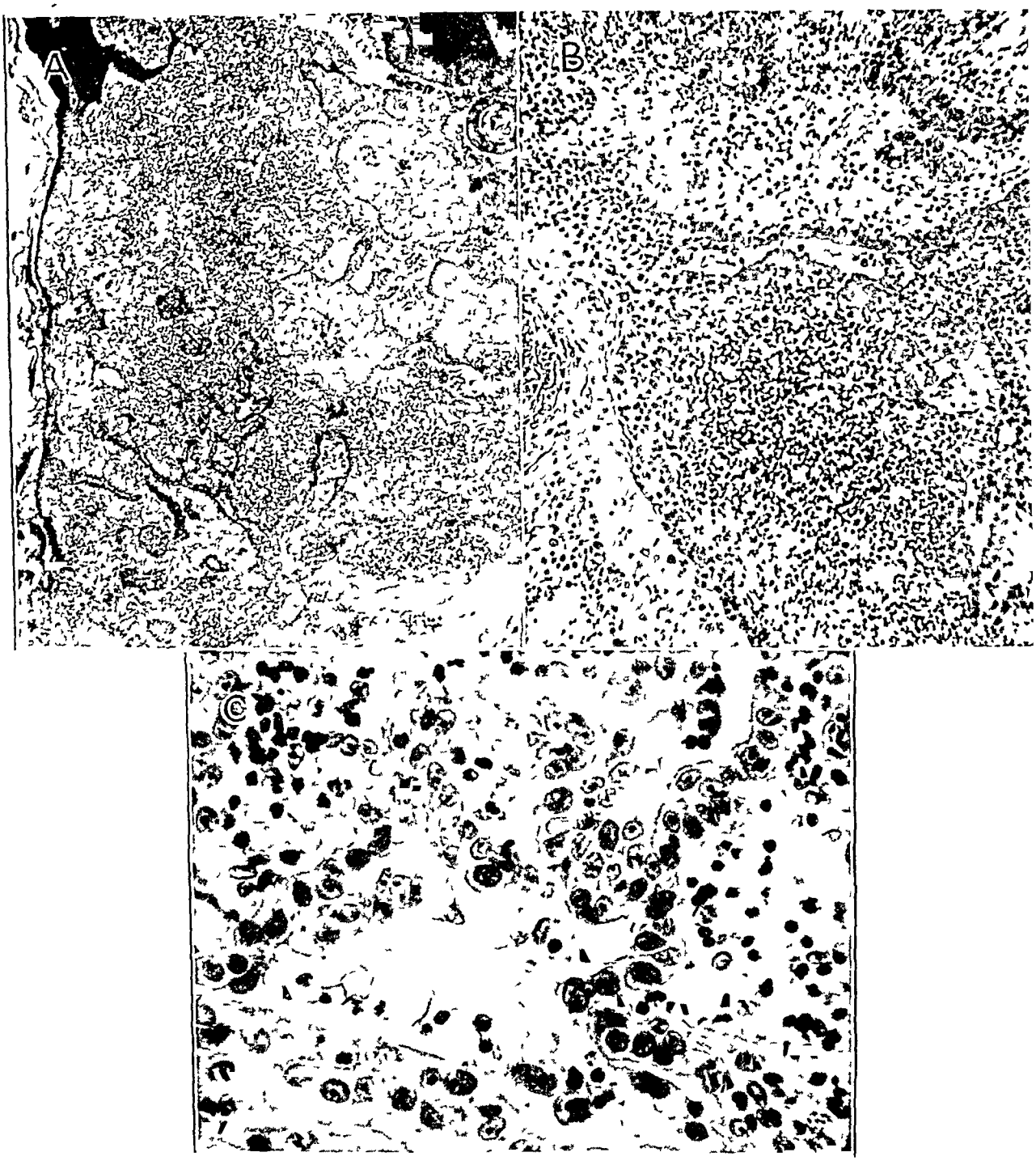


Fig 1—Transitional type (Different magnifications of the same tumor) *A*, low power view, showing a stratified squamous cell epithelioma infiltrating and forming atypical hair follicles, from which glandular structures originate *B*, medium power view, in which a portion of an atypical hair follicle with tubules in direct continuity with its basal layer may be seen *C*, high power view, showing sudoriparous structures, partially lined by a double layer of cuboidal cells

excess follicles are frequently encountered This observation, however, in our opinion, does not affect the hypothesis of the origin of these tumors from adnexal primordia any more than does the occurrence of "multiple points of origin" in other types of epitheliomas

We do not believe that the origin of these tumors can always be traced directly either to the basal cells or to an "initial mass between the basal layer and the rete" (Foot) Such an initial mass can occasionally be found in small tumors (particularly in the so-called "multiple flat epitheliomas") and may be interpreted as a peculiar type rather than as an early phase Foot's illustration of the earliest change [8] seems to resemble very closely what Allen illustrated as the "Jadassohn" type [9]

Although the initial point of origin cannot be determined in the majority of instances, we believe that Foot's concept, based largely on the ability of these tumors to differentiate, is logical and provides, as Arnold stated, "an integrated explanation of the basal cell carcinoma which accounts for its distribution, its variety of cellular patterns and its infiltrative but never metastasizing—habits of growth" [10] The formation of stratified squamous cell centers resembling frustrate hair follicles, in nests of so-called basal cell epitheliomas, indicates a higher degree of differentiation

The same holds true for "basal cell" tumors of the glandular type An understanding of all the transitional varieties, including the many cases in which a distinction between the pilar and sudoriparous type is well-nigh impossible, is greatly enhanced by assuming their common origin from adnexal primordia We have particular reference to the type of case in which the ribbon of so-called basal cells continues into a tubular-like structure, occasionally possessing a double lining, and to the primordial type resembling a solid hidradenoma The occurrence of true combinations, which we observed, also supports this hypothesis

We have not been able to follow Foot's classification of "basal-celled" tumor as a subgroup of adnexal carcinoma We believe that the majority of such instances may be regarded as of mixed tumors in which squamous cell epithelioma is superimposed at the epidermal margin of an eroding ulcer

There remains, however, a group of tumors which falls under neither of the previously discussed categories We have classified these growths as "transitional" tumors, which are anaplastic but which show certain features of both epidermoid and adnexal tumors With

8 Foot,[3] fig 8

9 Allen, A C, in Anderson, W A D Pathology, St Louis, C V Mosby Company, 1948, p 1235, fig 969

10 Arnold, H L, Jr Basal Cell Carcinoma of Sweat Gland Origin, Arch Dermat & Syph **57** 1042 (June) 1948

cells and resembling imperfect ducts or tubules We could not be certain in every instance whether these spaces resulted from degeneration or were manifestations of potential differentiation In these



Fig 2—Transitional (intermediate) type (Different magnifications of the same tumor) *A*, low power view, of islands of penetrating squamous cell epithelioma with growth of the basal cells in columns *B*, medium power view, showing an atypical follicle, a nest of anaplastic squamous cells and rows of basal cells *C*, medium power view, of squamous cell epithelioma, with the nest of a typical adnexal tumor indicated by *X* *D*, high power view of a portion of *C*

NODULAR VASCULITIS

ARTHUR R WOODBURNE, M D
AND
O S PHILPOTT, M D
DENVER

THE INCREASED interest and study of diseases of the blood vessels has brought to light many new syndromes which may be related or which may be separate diseases The study of such diseases as disseminate lupus erythematosus, periarteritis nodosa, scleroderma, cranial (temporal) arteritis [1] and migrating phlebitis [2] has centered interest on many points of similarity in these diseases A critical analysis of a group of cases observed in dermatologic practice in the light of our broader knowledge of vascular disease has stimulated this report Allen [3] has discussed this condition as a nontuberculous form of erythema induratum, which it simulates closely, however, its frequency and its lack of tuberculous causation warrant its distinction from the usual erythema induratum both by name and by more general knowledge The fact that we have been able to collect 6 cases during the past two years indicates that this is not a rare disease A review of recent dermatologic literature discloses only an occasional reference to this condition Montgomery, O'Leary and Barker [4] in their excellent article on nodular vascular diseases of the legs give a short discussion of the present problem, and Novy [5] suggests the underlying problem in the presentation of his case before the San Francisco Dermatological Society

From the Department of Dermatology, University of Colorado School of Medicine, Dr O S Philpott, professor, and from the practice of Drs O S Philpott and A R Woodburne, Denver Case 4 is from the clinical material of Dr Joseph D Friedland, Denver

1 Horton, B T , Magath, T B , and Brown, C E An Undescribed Form of Arteritis of the Temporal Vessels, Proc Staff Meet , Mayo Clin **7** 700-701 (Dec 7) 1932

2 Barker, N W Recurrent Idiopathic Thrombophlebitis of the Legs, M Clin North America **10** 597-599 (Sept) 1934

3 Allen, E V , Barker, N W , and Hines, E A Peripheral Vascular Diseases, Philadelphia, W B Saunders Company, 1946, pp 487-490

4 Montgomery, H , O'Leary, P A , and Barker, N W Nodular Vascular Diseases of the Legs , Erythema Induratum and Allied Conditions, J A M A **128** 335-341 (June 2) 1945

5 Novy, F G , Jr Case for Diagnosis (Erythema Induratum?), Arch Dermat & Syph **38** 997-998 (Dec) 1938

III *Mixed Type (Foot's "Basal Celled" Epithelioma)* Of the mixed type we have found approximately 20 cases The majority were of adnexal carcinomas, with areas of squamous epithelioma near the surface, which was invariably ulcerated Such cases should not be considered to belong to a subgroup of adnexal carcinomas, since they represent a combination of stratified squamous cell epithelioma and adnexal carcinoma, the former probably arising secondarily in the margin of an ulcer We have seen a considerable number of sections in which proliferative changes occurred in the epidermis overlying an adnexal tumor Very often one observes pronounced acanthosis, development of excessive numbers of follicles and occasionally evidence of varying degrees of dedifferentiation in the epidermis

Atypical proliferation of prickle cells and basal cells of the epidermis is not uncommon in adnexal tumors and does not justify the separation of such growths into a special type Not knowing whether or not the superficial stratified squamous epithelial cell component may not simply be secondarily induced, and being uncertain of its true pathogenetic relation to the adnexal type of tumor, we have chosen to refer to this group of tumors as "mixed carcinoma" of the skin, rather than as the "basal celled" type

IV *Transitional Carcinomas* There is in this series a significant number of cases, however, in which it appears difficult, if not arbitrary, to decide on an irrevocable classification It is not possible to determine accurately the frequency with which such transitional structures occur, since much depends on the willingness of the observer to admit the significance of variations from the classical picture Some of these intermediary tumors were classified under different terms at different times of reexamination These structures may be looked on as epidermoid cancers with basal cell features or as adnexal tumors with epidermoid features

A The epidermoid cancers with basal cell features are probably related to Darier and Ferrand's *épithéliome métatypique intermédiare* They consist of nests of squamous epithelial cells, often decidedly anaplastic, with atypical keratinization In some areas the bright red stained material can be identified as keratohyalin by its structural arrangement, and in other areas it resembles colloid material The characteristic feature consists of a budding of the basal layer, which becomes more or less independent and arranges itself in a lacelike network of strands and columns, resembling the "ribbon-like" bands or festoons in some forms of the adnexal carcinomas The cells, however, are larger, often cylindric and possess a light-stained cytoplasm, thus differing from ordinary so-called basal cells Also, high power magnification often disclosed a greater degree of disparity The resemblance to adnexal type of tumors is often evidenced by the expansile

in erythema nodosum They manifest a definite tendency to group along the course of, and to include in themselves, superficial vessels, occasionally there are bean-sized to walnut-sized chains of nodules along vessels The nodules heal without going through the bruise cycle so usual in erythema nodosum

Histopathologic study discloses a panvasculitis with little or no change in the epidermis and with a diffuse lymphocytic infiltrate in the dermis, more pronounced about the vessels and coil glands and in the vessel walls Aneurysmal pouches, necrosis or polymorphonuclear infiltration in the vessel walls is not apparent The vessels have thickened walls with swollen endothelial cells At the junction of the dermis and fat and in the fibrous trabeculae of the fat are large collections of lymphocytes and a few large mononuclear giant cells Some collections of epithelioid cells are seen deep in the sections Multinuclear giant cells may be seen in the deeper lesions, and a tuberculoid architecture is not unusual There is no caseation or necrosis Acid-fast or other organisms have not been found in any sections after prolonged study

REPORT OF CASES

Case 1.—D U, a girl aged 18, a student, gave the history of painful nodules of the legs for the past two years She had seldom been without one during this period, and an acute flare-up of the disease could be expected following tonsillitis Her family and personal history was otherwise noncontributory On physical examination she had, lateral to the midportion of the right tibia, a golf ball–sized nodular infiltrate, dusky red in color and moderately tender A similar, smaller nodule just above and medial to the left femoral epiphysis was noted She had cryptic and enlarged tonsils with pus in some crypts Roentgenograms of the teeth revealed normal conditions Examination of the blood and routine urinalyses gave normal results Sedimentation rate of erythrocytes on four occasions was 4, 2, 2 5 and 3 mm at the end of one hour (Cutler method) A complete tuberculosis survey, including roentgenogram of the chest, revealed normal conditions The tuberculin test gave a 1 plus reading The bleeding and the clotting time of the blood were normal This patient has been observed over a period of eighteen months, during which many episodes occurred Decided improvement occurred following tonsillectomy

Case 2.—R H, a man aged 30, had lost the right leg as the result of the explosion of a land mine Shortly after he was discharged from military service a painful nodule developed just above the internal malleolus of the left ankle Although this had gradually subsided, new nodules had developed later along the course of the external saphenous vein, each new nodule usually being an inch or so above the previous one When the patient was examined some eighteen months later he had a beadlike group of hickory nut–sized, dully inflammatory nodules on the lateral surface of the leg just below the knee and a group of three larger nodules medial to the knee in the lower portion of the thigh Otherwise, physical examination revealed nothing unusual Various laboratory observations were made The sedimentation rate was 11 5 and 11 mm per hour

hair follicles, were seen to originate from nests of keratinizing anaplastic prickle cells

B Adnexal tumors with epidermoid features were characterized mainly by the appearance of atypical, laminated squamous cell elements in the center of primordial nests, occasionally, however, these prickle cells appeared in large nests as vacuolized elements resembling sebaceous cells These cases were difficult to distinguish from those of true transitional tumors, and they may represent a malignant variety of the pilar type proper of adnexal carcinoma

Transitional tumors, of which we have seen only a small number, show areas of both the adnexal and the epidermoid type of tumor blending into each other Unless serial sections are made, it is difficult to determine whether or not such cases belong to what we have referred to as mixed tumor Only those instances in which the complex tumor develops underneath an intact epidermis should be regarded as transitional

COMMENT

The study of our material has impressed us with the frequency with which borderline neoplasms resist a clearcut classification as basal cell, basal-squamous cell or squamous cell epithelioma. Many cases had to be squeezed into the given "pigeon holes" by overemphasis of the quantitative preponderance of certain types of tumor cells or structures

The greatest difficulty was encountered in the group of so-called basal-squamous cell epitheliomas characterized by the appearance of squamous epithelial elements in the center of basal cell nests The histologic pattern, aside from this sign of differentiation, resembles too closely that of other basal cell tumors to warrant the segregation into a special oncologic entity The term basal-squamous cell epithelioma implies that these basal cell tumors also possess characteristics of squamous cell epithelioma, an implication for which there is no support The squamous epithelial cells are not seen to infiltrate independently in small groups or as isolated cells but always remain within their mantle of basal cells The resemblance to abortive hair follicles, on the other hand, is apparent

Montgomery [7] commented that the finding of normal adult follicles in a section showing no connection with the basal cell growth is not compatible with Foot's hypothesis It is true in our own observation that numerous adult follicles are often seen in conjunction with the adnexal tumors They are not always "pushed" aside, and, moreover,

7 Montgomery, H, and others Atlas of Dermal Pathology, prepared [at the Army Institute of Pathology] by the Registry Committee on Dermal Pathology of the American Academy of Dermatology and Syphilology, Washington, D C, Registry Press, 1947, pp 48-49

abnormal A nodule removed from the lateral surface of the left leg for microscopic study illustrated the general features already described

CASE 4—Mrs E I, aged 54, had had recurrent, painful nodules of the lower portion of the legs for five years Examination revealed a bluish red nodule 2 by 3 cm lateral to the left tibia opposite the junction of its lower and middle third This nodule was deeply infiltrated, tender and apparently involuting A more recent nodule was seen just below the right knee Tissue was removed



Fig 3 (case 6) —Gross appearance of characteristic nodular lesion (× 17 5)

from this area for study (figure 2) Laboratory studies gave normal results There were no depressed areas, scars or atrophy indicating sites of previous lesions A survey for tuberculosis which included roentgen examination of the chest and tuberculin tests disclosed normal conditions

CASE 5—Mrs E T, aged 60, had multiple nodules in linear arrangement on the lower part of both legs and scattered groups on both thighs This patient had an anal fistula and had experienced persistent diarrhea with recurrent

the acceptance of Foot's theory, some such neoplasms may justly be classified as primordial carcinomas of a high degree of malignancy.

SUMMARY

Clinical data concerning 1,257 patients with epitheliomas are presented Half of all the lesions occurred in persons between 50 and 69 years of age Men presented 53 7 per cent of the basal cell lesions and 67 2 per cent of the squamous cell variety The occupational environment of 42 5 per cent of the patients was outdoors Almost half of the patients waited from one to three years before seeking treatment Of the series of lesions, 46 8 per cent had a surface diameter of more than 1 cm Two thirds of the lesions occurring on the ear, jaw and hand were in men, whereas two thirds of the epitheliomas of the forehead, nasolabial area, chin, arm and leg appeared in women While a majority of the lesions were of the basal cell variety, it did appear that, as the size of the lesions increased, the squamous cell type was found more frequently Blonds had 84 4 per cent of all the lesions The concept of an etiologic relationship between solar radiation and epithelioma is given additional support

A histologic review of 968 epitheliomas is presented Foot's concept of adnexal primordium as the focus of origin of so-called basal cell tumors is considered a satisfactory explanation of epitheliomas with transitional and mixed features.

403 North Tryon Street (Drs Welton and Elliott)

1400 Scott Avenue (Dr Kimmelstiel)

DIFFERENTIAL DIAGNOSIS

With previously noted positive points in physical and laboratory diagnosis kept in mind, we shall attempt to indicate points of differentiation between nodular vasculitis and other nodular lesions of the legs

1 Lesions of erythema induratum (tuberculous type) are rarely painful and are only slightly tender, usually on the dorsal surface of the

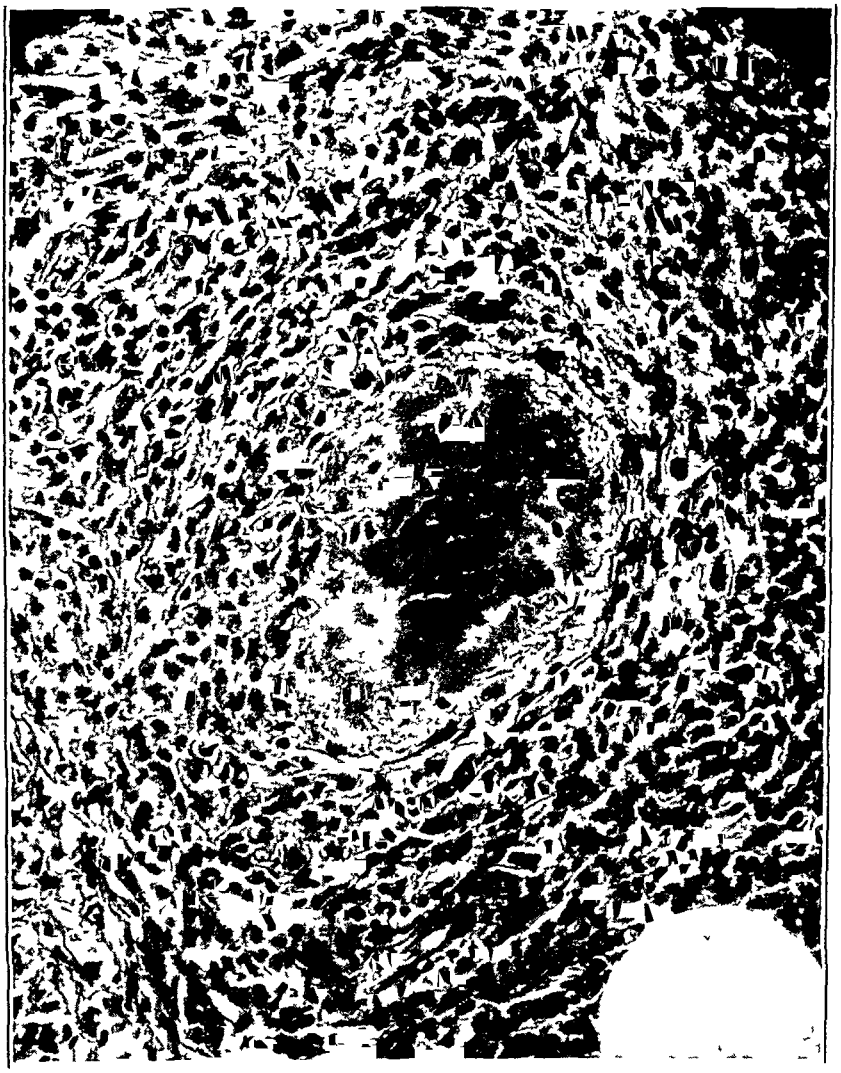


Fig 5 (case 6) —Tissue taken lower in the section presented as figure 3 reveals a large collection of lymphocytes, occasional mononuclear cells, fibroblastic proliferation and a multinuclear giant cell (× 330)

calf Ulceration is usual, and the inflammatory reaction is chronic The tuberculin test gives positive results, and the microscopic architecture of the lesions is that of tuberculosis

2 Lesions of erythema nodosum (*sui generis*) develop in a single crop Although recurrences have been observed, they are not usual The inflammatory reaction, pain and tenderness are acute and are usually

The general picture of nodular vasculitis is that of a healthy person between the ages of 13 and 60, with a history of recurrent, mildly painful and tender nodules of the anterior surface of the leg with occasional nodules of the thigh and upper extremities The individual nodules persist for several months, and new lesions develop at intervals of one or two months The disease lasts from a few months to several years, and nodules heal without atrophy, scarring or depression of the

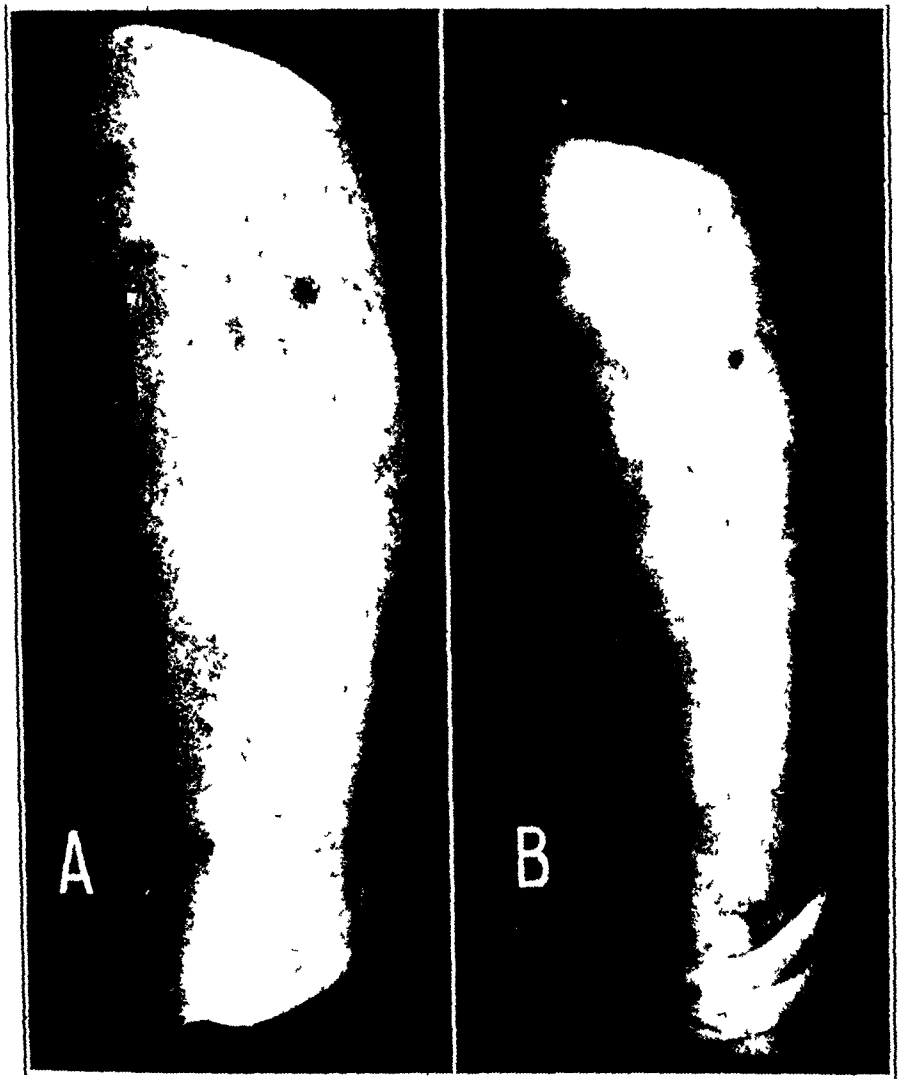


Fig 1 (case 6) —*A*, typical clinical picture in nodular vasculitis, *B*, infra-red photography of the same lesion Note the association of nodules and superficial vessels

surface New crops of lesions do not manifest a tendency to occur in cold weather Changes in temperature and season do not seem to have an influence on lesions

On physical examination the nodules resemble most closely those of erythema nodosum, being dusky red, mildly painful, moderately tender and usually seen on the anterior portion of the leg These nodules do not, however, show capital points of extreme tenderness as is usual

scopic study shows the pathologic process to be located in the subcutaneous adipose tissue Healing occurs with replacement of fat by fibrous tissue and depression of the superimposed dermis and epidermis It may be that nodular vasculitis is closely related to this syndrome However, since the inflammatory reaction in nodular vasculitis is in the dermis, healing that occurs by fibrosis does not result in depression of superior tissues

9 Periarteritis nodosa manifests as a rule smaller nodules, more evidence of involvement of internal organs, and a microscopic display of aneurysmal dilatation of vessels, polymorphonuclear infiltration and necrosis of vessel walls Periarteritis nodosa has been reported as an allergic response to various agents, occasionally to the sulfonamide compounds

10 Sarcoid as a rule exhibits fewer nodules and less inflammatory reaction, the nodules are usually painless Microscopic examination will exclude this condition

11 Sarcoma is usually a single tumor or appears in a single group This disease displays no inflammation and has a characteristic microscopic picture

TREATMENT

Treatment in nodular vasculitis has been as a rule unsatisfactory Prolonged rest in bed with elevation of the legs and the application of warm or cool compresses have been the most generally helpful measures Removal of foci of infection has seemed to be of importance in other instances In case 1 improvement was rapid after the removal of infected tonsils, in case 6 the patient responded well to the extraction of an abscessed molar Web or elastic support to the lower part of the legs has been helpful in some instances Allen [3] has obtained good results with the use of a streptococcus vaccine in ascending doses below the level productive of reactions The antibiotic agents have seemed to be of help at first but have never produced permanent improvement Large doses of salicylates have made the patients more comfortable and have seemed to aid involution of the lesions in several cases

SUMMARY

Six cases of a nodular, moderately painful and tender eruption of the legs are reported The differential diagnosis and pathologic features of the eruption are discussed, and some observations on etiology and treatment are made It is our opinion that nodular vasculitis is a definite clinical and pathologic syndrome which is not rare It may be related to periarteritis nodosa or nodular nonsuppurative panniculitis, but it should be recognized and separated from other more generally recognized nodular disturbances of the legs and thighs

434 Metropolitan Building

Results of a complete examination of the blood and urinalysis were within normal limits on several occasions, the Kahn test was negative, the tuberculin test gave a reading of 1 plus and roentgen examination of the chest revealed normal conditions We were able to observe this patient through several episodes Administration of penicillin in large doses for four weeks did not produce well defined change in the nodules Use of sulfonamide compounds over a long period also proved ineffectual

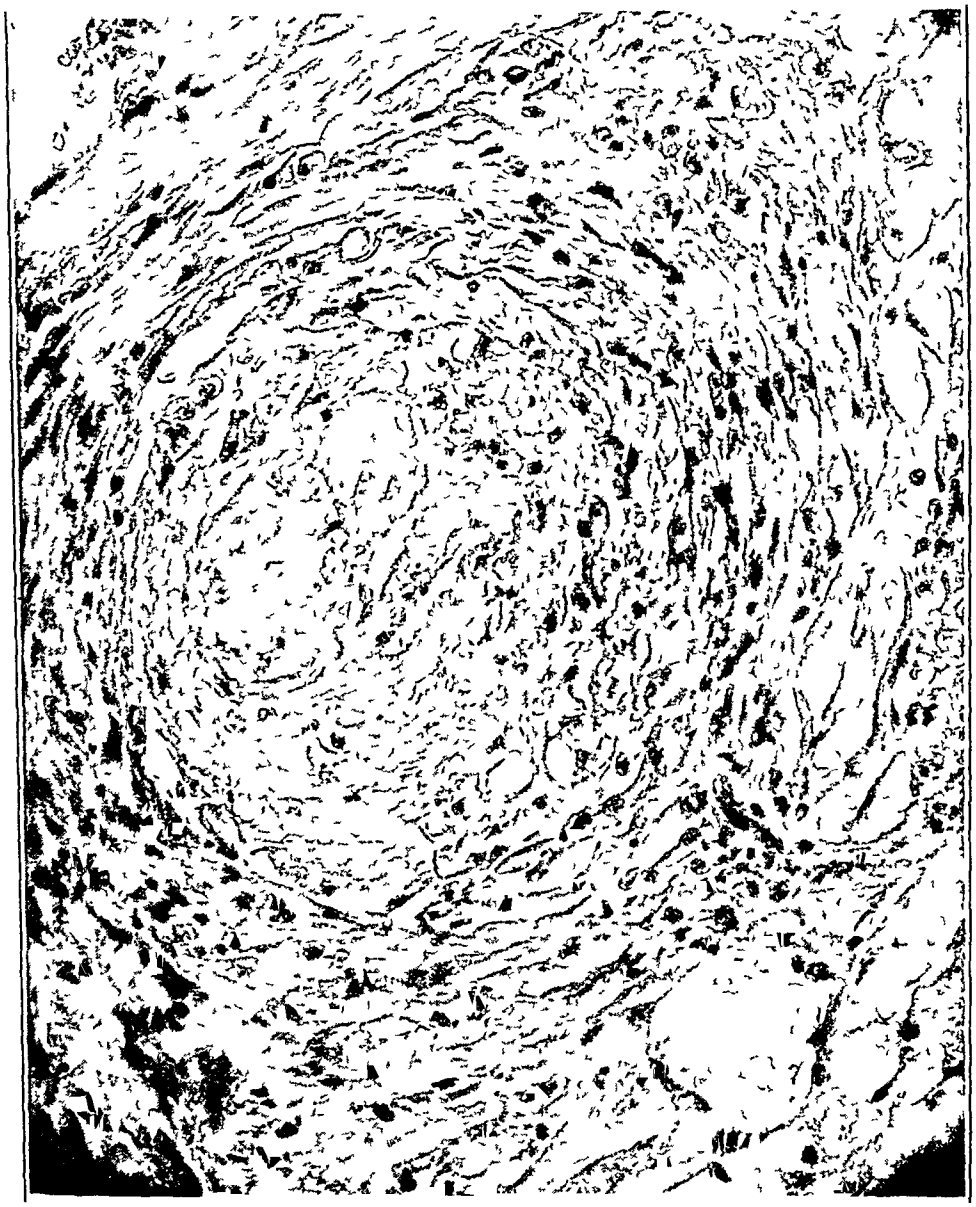


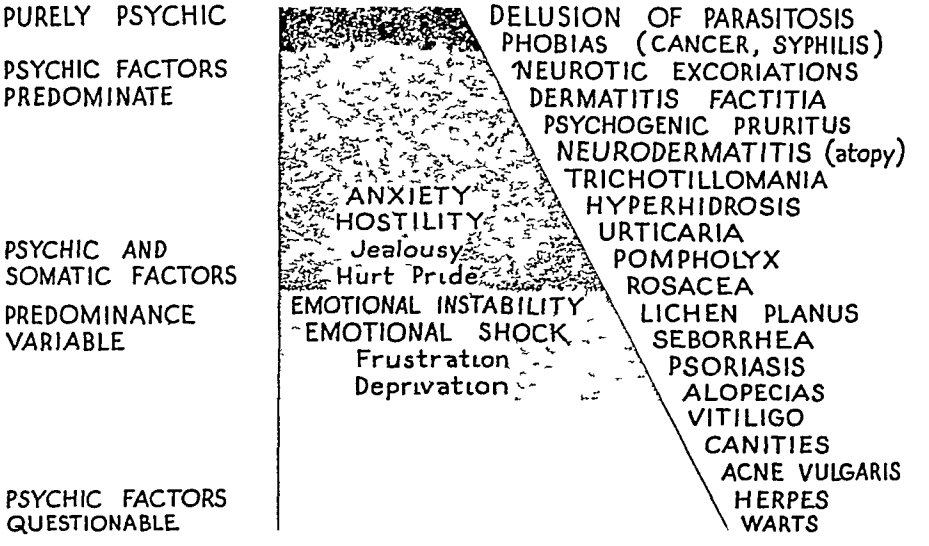
Fig 2 (case 4) —Photomicrograph from deep dermis exhibits features similar to those in figure 5 but with more epithelioid cells (× 330)

Case 3—G B, a girl aged 14, had multiple, recurrent, painful nodules of twelve months' duration on the anterior portion of the legs and thighs Five episodes of this condition were reported Physical examination disclosed scattered nodules of the anterior surface of the legs, eight groups of two or three nodules and one or two single nodules, one single nodule of the lateral area of the left thigh and one of the left arm Results of laboratory tests were not grossly

best modifiable only with deep-going methods of psychotherapy Other cases are mild, and in such cases an impressive examination followed by an unambiguous statement of physical normality may be sufficient for cure or adequate amelioration of the condition

For patients with self-inflicted lesions such as neurotic excoriations psychiatric aid is usually necessary, but with self-inflicted lesions produced for a definite purpose such as getting attention or arousing sympathy, unraveling the underlying cause may suffice to prevent further demonstration

In the study of neurodermatitis made by Walsh and Kierland [4] at the Mayo Clinic, conscientious psychotherapy was administered to 15 patients In 3 patients with pronounced depressive reaction a series of electric shock treatments was also given With 1 exception (a



Stereoscopic diagram of the psyche and soma in dermatology

patient in whom there was failure because of a language difficulty) improvement in the emotional disorders was paralleled by a complete or nearly complete clearing of the dermatologic reaction, the improvement endured for the period of observation in all patients whose dermatologic reaction first appeared in adult life

Psychogenic pruritus may also be a problem for the psychiatrist In a physician aged 50 who was treated at the Temple University Hospital for an intolerable pruritus for which no somatic cause could be found, electric shock therapy brought about a complete and lasting cure after the patient failed to respond to local therapy, diet, sedatives and psychiatric consultation

4 Walsh, M N, and Kierland, R R Psychotherapy in the Treatment of Neurodermatitis, Proc Staff Meet, Mayo Clin **22** 578 (Dec. 10) 1947

episodes of colitis accompanied with the development of nodules during the past eighteen months Laboratory studies revealed no evidence of tuberculosis

CASE 6—Mrs R W S, aged 38, had had recurrent, painful and tender nodules of the lower portion of the legs for eight months These began as small, oval, tender areas New lesions had developed periodically The first group was at the junction of the lower and middle third of the left leg This group consisted of four confluent nodules each about 1 5 cm in diameter During the

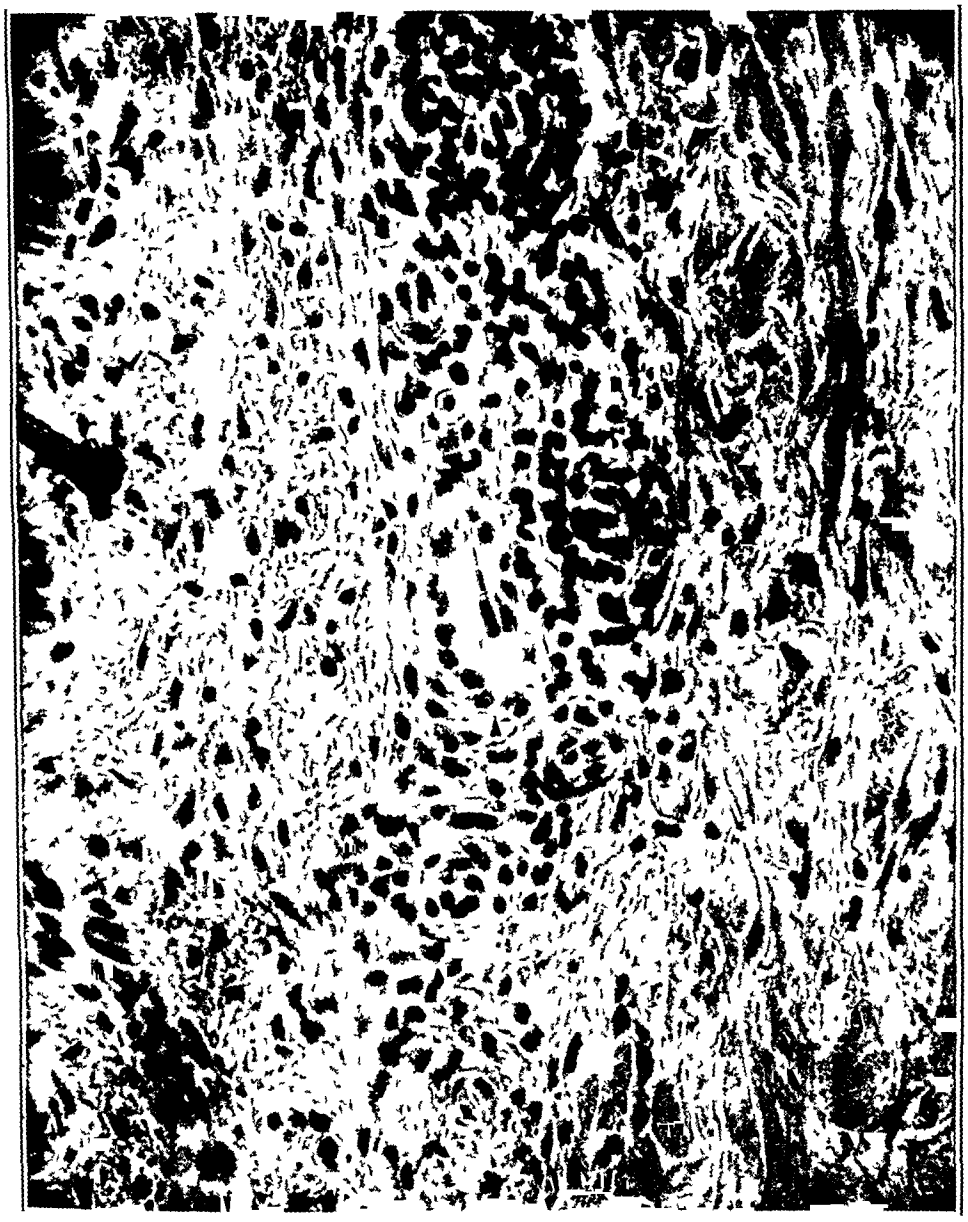


Fig 4 (case 6) —Section from dermis of lesion in photomicrograph 3 exhibits characteristic diffuse lymphocytic infiltrate with focal collection about vessels in the center (× 330)

period of observation five or six other small nodules developed over the upper part of the left leg, with two small nodules on the anterior and lateral surface of the left leg Two nodules were removed for microscopic examination (figs 3, 4 and 5) Infra-red photography has shown the close association of these nodules with superficial vessels

distress and symptoms The psychiatrist has found that time to allow for reorientation in thinking is important and that a speedy solution to emotional problems is infrequent Hence, there is no reason to be discouraged with psychotherapy because it does not remove the patient's symptoms immediately Dermatology and psychiatry may seem to be widely separated specialties, but they have in common a few acute manifestations of symptoms and many chronic ones which yield slowly to therapy

When the dermatologist has definitely or with reasonable assurance made up his mind that he is dealing with a psychosis, it becomes necessary to make the patient accept the idea that a psychiatrist should be consulted This is by no means easy, and the following steps are suggested (1) inform the family rather than the patient of your diagnosis, (2) consult with the family regarding the possible reaction of the patient when told of such a diagnosis, (3) get the opinion of the family or some member of the family as to whether they or you should make the disclosure If the problem of referral to a psychiatrist is not handled carefully, dissatisfaction on the part of both patient and family is apt to result, with complete loss of confidence in the dermatologist and eventual therapeutic failure

associated with an acute infection of the upper part of the respiratory tract or with rheumatic disease Erythema nodosum is a self-limited disease, seldom of longer duration than six weeks, and it occurs usually in young girls Individual lesions progress through the bruise cycle as they heal

3 Erythema nodosum (symptomatic) is associated with the following conditions

A Tuberculosis Nodules occur in young persons 10 to 18 years of age, associated with or following the primary tuberculous complex, with a negative response to the tuberculin test early in the disease and a positive result during or following the nodular episode

B. Coccidiomycosis The nodules develop a short time after an episode of pulmonary coccidioidomycosis ("valley fever"), the coccidioidin skin test becomes positive during or after the nodular episode

C Leprous erythema nodosum Leprous erythema nodosum is found associated with the lepromatous form of leprosy, nearly always during periods of activity in which arthritic, neuritic and other evidence of the disease exhibit a definite exacerbation

D Diphtheria Diphtheria may exhibit nodules simulating erythema nodosum associated with angina, membrane and positive throat culture

E Measles Occasionally nodules of this type are seen with and following the typical eruption of measles

F Drugs Drugs may produce lesions simulating those of erythema nodosum Iodides and bromides in particular are responsible Lesions due to drugs usually are more transitory, and a history of ingestion of the medicament can usually be obtained

4 Thrombophlebitis follows the course of superficial veins and extends proximally along them Tests of these veins reveal that they are occluded

5 Tularemia nodules may be mistaken for those of erythema nodosum but are usually more acute and break down early, the presence of bacteria may be demonstrated, and agglutination tests become positive

6 Nodular tertiary syphilis exhibits early ulceration, serpiginous outline, soft scarring with hyperpigmentation of borders and a positive response to serologic tests

7 Chilblain is usually located over bony prominences or the achilles tendon, the peripheral circulation is easily influenced by changes in temperature, and there is a history of onset and exacerbation in cold weather

8 Nodular nosuppurative panniculitis (Weber-Christian disease) is characterized by deeper nodules with recurrent crops associated with fever and healing with depressed areas of legs and thighs The micro-

rheic dermatitis is a concept difficult to accept To me it seems easier and more satisfactory to hold to a view of neurodermatitis (atopic dermatitis) sufficiently broad to accept almost all forms of dermatitis seen in this region Immediately, one meets the difficulty of lack of general agreement as to terminology, classifications are arbitrary, and one may be satisfied to call this localized neurodermatitis At the outset one may properly inquire whether this eruption deserves consideration separate from other localized manifestations of neurodermatitis, but I think the question should not be answered before the facts have been set out Through this discussion I shall use the term neurodermatitis as synonymous with atopic dermatitis

In preparing this presentation I have reviewed the records of a consecutive series of 83 patients with dermatitis localized to, or beginning in and extending from, the suboccipital fossa The patients are divided into two groups group A, those whose eruption was limited to the area under consideration (49 patients), and group B, those who had other manifestations of neurodermatitis (34 patients) Patients with vulvar or anal dermatitis were excluded from this study The cases will be discussed with reference to clinical features, histologic manifestations, therapeutic response and etiologic considerations During the same period I saw only 2 male patients with similar eruptions Their eruptions were of long duration and responded poorly to treatment

CLINICAL FEATURES

Dermatitis of the suboccipital fossa is sometimes referred to as lichen simplex chronicus, yet a review of the clinical features soon demonstrates the inaccuracy of general use of this appellation The inflammatory reaction is more active than is that in ordinary lichenification, and there often are excoriations, traumatic dermatitis, superficial infection and dermatitis resulting from ill advised therapeutic applications Next to itching, redness was found to be the commonest clinical feature and was usually associated with thickening and frequently with scaling, less often with crusting and excoriation Clearcut lichenification was evident in only one fourth of the cases with eruptions limited to the single site, and was even less frequent when the patient presented other evidences of eczema When not lichenified the eruptions remained relatively dry and the tendency to moistness was seen usually as a result of excoriation rather than in the form noted in nummular eczema, for instance Lichenification was observed in 1 case in which the eruption had been present for six months, but it usually was present only when the disorder had lasted a year or more Formation of a plaque was almost constant, with discrete papular elements observed infrequently Unilateral involvement was relatively rare There was considerable variation in the extent

THERAPY OF PSYCHOSOMATIC DERMATOSES

CARROLL S WRIGHT, M D
PHILADELPHIA

TO CLASSIFY a dermatosis among the psychosomatic disorders of the skin is not always difficult, but treatment may prove to be a real problem A study of the accompanying chart [1] may aid in the decision as to the best method of management in a given case The diseases listed (delusion of parasitosis, phobias [cancer, syphilis], neurotic excoriations, dermatitis factitia, psychogenic pruritis, neurodermatitis [atopy], trichotillomania, hyperhidrosis, urticaria, pompholyx, rosacea, lichen planus, seborrhea, psoriasis, alopecia, vitiligo, canities, acne vulgaris, herpes and warts) range from the purely psychic to those in which psychic factors are questionable

Disorders of the skin that are purely psychic will usually require psychiatric treatment to the exclusion of the dermatologist once a diagnosis is made, whereas those in which psychic factors predominate may primarily require treatment by a psychiatrist with perhaps considerable aid from the dermatologist As the shading in the chart lightens, there is a corresponding lessening in the degree to which the patient may be mentally ill, with the result that treatment by the dermatologist becomes increasingly important It may be helpful to discuss individually some of the diseases listed in the illustration

Wilson and Miller,[2] to whom I am indebted for separating out cases designated as delusion of parasitosis from the phobias, point out that the psychiatrist occasionally the dermatologist rarely succeeds in curing the delusion They recommend modern electric shock and insulin shock therapy as employed by psychiatrists as most likely to improve the prognosis considerably in certain groups

Levine [3] believes that some phobias of disease, notably syphilis and cancer, are deep-seated and persuasive and may be unmodifiable or at

From the Department of Dermatology and Syphilology, Temple University School of Medicine, and the Skin and Cancer Hospital

1 Psychosomatic Medicine in Relation to Dermatology, read before the Southern Medical Association, Miami, Florida, Oct 27, 1946

2 Wilson, J, and Miller, H E A Delusion of Parasitosis (Acarophobia), Arch Dermat & Syph **54** 39 (July) 1946

3 Levine, M Psychotherapy in Medical Practice, New York, The Macmillan Company, 1942, revised 1945

SEBORRHEA

Mild seborrhea, which was noted in approximately half the patients, is found in a proportion not greatly different from that for the entire population Certainly, the incidence should be much higher and the inflammation severer if seborrhea were important in causing dermatitis at this site

MENSTRUAL HISTORY

An abnormal menstrual history is frequently given by patients with "functional" disorders Criteria of abnormality are difficult to establish but in this instance were arbitrarily selected, frequency of menstruation of less than twenty-four or more than thirty-two days, duration of less than four or more than six days or amounts spoken of as "scant" or "profuse"

Table 3 shows clearly that abnormal menstruation occurs much more frequently among women with suboccipital dermatitis than among

TABLE 3.—*Association with Abnormal Menses*

Age, Years	Groups A and B	All Patients with Any Type of Neurodermatitis
Total	49	455
Less than 20	27%	17%
20 to 40	45%	27%

all women with neurodermatitis The presence of normal menstruation is of greater significance than is a history of abnormality in women over the age of 40 years Above that age, normal menstruation is twice as common in all patients with neurodermatitis as in those with suboccipital dermatitis It is concluded that there is a significant association between suboccipital dermatitis and ovarian dysfunction

MICROSCOPIC PATHOLOGY

Histologic examination might have been expected to provide evidence for accurate differential diagnosis, but it did not, as I discovered on study of 29 specimens taken for biopsy and comparison of them with other specimens, of psoriasis of the scalp and seborrheic dermatitis The difficulty lies not in the site involved but in the nature of the processes to be differentiated Gans [3] pointed out differences in lichenified neurodermatitis, eczema and seborrhea, but the attempt seems forced, and the discussion is generally unsatisfactory MacCardle and the Engmans [4] listed detailed features and concluded that they

3 Gans, O Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925, vol 1, pp 245, 263 and 275

4 MacCardle, R C, Engman, M F, Jr, and Engman, M F, Sr Histology of Neurodermatitis, Arch Dermat & Syph **44** 161 (Aug) 1941

Psychiatric help may also be required for trichotillomania, which is often regarded by the psychiatrist as a form of masturbation, although proper approach by the dermatologist may result in cure Other types of hair loss such a alopecia areata and general thinning of the hair, which may at times ocur after nervous shock or prolonged emotional disturbances, usually respond to dermatologic therapy The same applies to the intermittent type of hyperhidrosis, although at times this may be a true psychiatric problem

In the intermediate group of diseases in which psychic and somatic factors vary in their predominance, the emotional factor is seldom deep and can usually be managed by the dermatologist For example, psoriasis, which is considered incurable, will often clear completely with freedom from the disease for variable and often prolonged periods of time If the possibility of this relief is explained to the patient instead of using the commoner approach and stating that "psoriasis is incurable," improvement or even temporary "cure" may be obtained rather than loss of faith in ethical medicine and resultant compromise with advertised patent remedies

Vitiligo, canities and warts have been placed at the bottom of the list, for there is little or no proof that psychic factors have any real causative effect Whether warts respond to psychotherapy is in my opinion still controversial, because they are known to be due to a virus and virus infections will usually disappear spontaneously in time

Success or failure in the treatment of psychosomatic disorders is often dependent on the first consultation between the patient and the physician The physician who has no sympathy with nervous manifestations and takes a hostile attitude or manifests a frank disinterest in this phase of his patient's disease will usually fail in his therapeutic efforts Vice versa, the quick assumption that nervous factors are solely to blame and failure to make a thorough search for physical causes may also result in therapeutic failure

When psychotherapy is introduced in the treatment of cutaneous conditions, efforts to treat the skin itself are being relaxed and a new element is introduced for the discovery of precipitating factors, this procedure doubtless often makes a contribution toward correction of the underlying exhaustion One does not then rely so much on drugs and other treatments applied to the skin, but thoughts of physician and patient are turned toward the mental irritations which may be finding their way to the skin either through the phenomenon of conversion involving symbolization or through well known pathways of the autonomic nervous system to pervert circulation, glandular activity or both, or to cause trophic changes

If the physician looks sympathetically and helpfully for nervousness as an etiologic factor, the patient will generally help and with each visit will bring added information or clues as to the relation of emotional

ciated with elongation or clubbing of the rete pegs Epithelial edema was commonly present, but only in slight to moderate degree and in only 5 instances was there anything even slightly resembling vesiculation Frequently one noted degeneration of individual cells or groups of several cells in the rete layer When lymphocytes invaded these areas of degeneration, there was sometimes more edema and thus the development of a minute vesicle Lymphocytes were occasionally noted singly or in groups of two or three, but no epithelial abscesses were observed The cutis frequently presented some edema The connective tissues often appeared swollen and fragmented Special



Fig 2—Section showing more acute inflammation with disarrangement of structure, more parakeratosis and more and deeper infiltrate than are shown in figure 1 Seldom were such changes noted in suboccipital dermatitis

stains showed that the elastic tissue was often greatly decreased or fragmented, the collagen fibers were frequently degenerating and fragmented even though the eruption had not been present long Capillary dilatation was commonly present and was frequently associated with congestion Thickening of the walls of larger vessels is difficult to evaluate but seemed to be present in 10 instances Cellular infiltrate was always present and consisted almost exclusively of lymphocytes oftener small than large Frequently there were aggregations of young or wandering connective tissue cells A few polymorphonuclear leukocytes were also present in many instances Eosinophils were rare and red blood cells were seen only occasionally The

Archives of Dermatology and Syphilology

VOLUME 60 SEPTEMBER 1949 NUMBER 3

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SUBOCCIPITAL DERMATITIS

FRANCIS W LYNCH, M D
Clinical Professor, Division of Dermatology, University of Minnesota
ST PAUL

SUBOCCIPITAL dermatitis is presented frequently in every clinic or office and is a disorder of ill repute in that it is usually regarded as a stubborn and nonresponsive member of that notoriously difficult family, eczema Discussion of dermatitis of the suboccipital fossa when spoken of at all, the disease is called lichen simplex chronicus of the nape is almost uniformly avoided by authors of standard textbooks Duhring merely stated that the nape is a common site for eczema in the young or the old Savill [1] offered a slightly more extensive discussion, though I disagree with her statements that "only rarely is there found a degree of moisture" She expressed the belief that the condition is largely due to the habit of scratching and said, "It provides a form of psychological relief from worry and mental tension" With reference to neurodermatitis, Barber [2] stated that "the most characteristic site, perhaps, is the nape of the neck, since here it is almost peculiar to women" He strongly advocated estrogenic therapy Many papers on lichen simplex chronicus give brief reference to dermatitis of the nape or suboccipital fossa My present concern is with two factors (1) whether most instances of suboccipital dermatitis should be regarded as neurodermatitis and (2) whether neurodermatitis in this location has any important features different from those of neurodermatitis in general

Clinicians have expressed various opinions as to the cause and nature of the chronic, inflammatory reaction frequently observed below the occipital prominence Some have regarded it as psoriasis and others as seborrheic dermatitis, contact dermatitis or atopic dermatitis (neurodermatitis) For the first three of these diagnoses there seems inadequate evidence, also, one would have to make different diagnoses for various manifestations which are observed at that site Differentiation of psoriasis is usually not difficult, since other more or less distant manifestations are of considerable assistance Contact dermatitis seems to me rather easily recognized Circumscribed sebor-

Read as the presidential address at the annual meeting of the Chicago Dermatological Society, Jan 21, 1948 Introductory comments have been deleted

1 Savill, A The Hair and Scalp, ed 3, Baltimore, Williams & Wilkins Company, 1945, p 146

2 Barber, H W Dermatoses of the Menopause, Practitioner **156** 333, 1946

during the waking hours Estrogens were not prescribed unless the patient was in the postmenopausal period or gave a history suggesting estrogenic deficiency, estrogens were sometimes given by injection but more often orally, in the form of diethylstilbestrol, 0 25 to 1 0 mg , or estrogenic substances, water soluble (premarin®), 1 25 mg , on retiring Their chief effect is probably by way of general relaxation and related emotional mechanisms rather than by direct chemical and physiologic influences on the skin

RESPONSE TO THERAPY

Therapeutic response was analyzed in those cases in which there was sufficient observation Table 4 gives the results in each group, those without and those with other eczematous manifestations In the first group the records of 36 cases were reviewed, and in 30

TABLE 4.—*Response to Treatment*

Duration of Disease Previous to Treatment	Good Results			Fair	Recurrences	No Response
	Within 2 Mo	At 2 to 4 Mo	After 4 Mo			
	Group A					
Less than 3 mo	2	3		2		2
3 to 6 mo	1	1				1
6 to 12 mo	4					
More than 1 yr	7	3		1	3	
Total—30	14	7	0	3	3	3
	47%	23%		10%	10%	10%
	Group B					
Less than 3 mo	4			2		
3 to 6 mo		1			2	
6 to 12 mo	1		1			
More than 1 yr	2		1	5	4	
Total—23	7	1	2	7	6	
	30%	4%	9%	30%	26%	0%

the data were sufficient to lead to the conclusions presented in table 4 (group A) Complete failure to influence the disease was noted to be infrequent, occurring in 10 per cent, and not related to previous duration of the illness Prolonged, complete or almost complete relief occurred commonly, also regardless of previous duration Among the women with additional neurodermatitis, cure was found to be much less likely 13 versus 70 per cent especially among those who had suffered previously for six or more months (table 4, group B) The last group of women also provided many more examples of recurrence following an initially favorable response and many patients who gained moderate improvement rather than really good results

In general, the response to therapy was reasonably favorable The recorded clinical notes give somewhat inadequate information as to the reasons for recurrence or failure, and yet two conclusions seem

of the eruption, but in most instances the plaque was practically limited to the fossa and its margins, being 1 to 2 inches (2 5 to 5 cm) in diameter

AGE

Investigation of ages of patients with suboccipital dermatitis showed that there is no significant difference between the age at onset in these two groups and in 738 female patients with neurodermatitis of other types There was some decrease in incidence in the first and second decades of life and an increase in the 30 to 40 year age group, but these differences were not great

TABLE 1—*Ages of Women with Neurodermatitis*

Age, Years	Group A	Group B	All Patients with Any Type of Neurodermatitis
Total	49	34	738
Less than 20	14%	9%	15%
20 to 40	46%	45%	43%
More than 40	40%	43%	41%

TABLE 2—*Association of Neurodermatitis with History of Atopy*

Age, Years	Group A	Group B	All Patients with Any Type of Neurodermatitis
Total	34	29	592
Less than 20	67%	67%	58%
20 to 40	70%	73%	63%
More than 40	50%	91%	50%
Average	62%	75%	58%

ATOPY

Patients were questioned for information relative to other recognized personal atopic disorders (hay fever, asthma or eczema in infancy or early childhood) and for the presence of these diseases in closely related members of their families Of all female patients with neurodermatitis, there was a history of one or more of these features in 58 per cent, while 70 per cent of patients with suboccipital dermatitis gave such histories Concerning the obvious inaccuracy of replies to such questions, I question whether this difference is significant

For persons in group A over 40 years old the positive histories were fewer, even though added years had provided more time for atopic manifestations to become evident The significance of these lowered figures need not be discussed since they are characteristic for all women with neurodermatitis

results were less satisfactory when this eruption was accompanied by neurodermatitis at other sites, improvement was less likely to be really satisfactory, and recurrences were oftener observed Estrogenic therapy is regarded as a valuable adjuvant when there are any other indications for its use Emotional and psychologic factors seemed particularly important in those patients who did not improve Treatment often included mild sedation and the use of some of the psychotherapeutic attempts of the nonpsychiatrist

At the outset, this discussion avoided consideration of the question whether suboccipital dermatitis deserves analysis as a more or less separate entity It appears to present many similarities to keratoderma climactericum Each occurs almost entirely among women and frequently presents clinical features of subacute dermatitis as well as lichenification Each disorder is commonly associated with evidence of estrogenic deficiency (or related endocrine factors) but is by no means limited to the climacteric age group These endocrine factors appear to be more constantly evident among those women with palmar or plantar dermatitis, but in each group the therapeutic response is more likely to be favorable when estrogens are used Psychologic and emotional factors seem clearly evident in both conditions, and to me both appear to be forms of neurodermatitis If one regards neurodermatitis as always due to a complexity of causes rather than to a single agent or mechanism, then these two disorders (keratoderma climactericum and suboccipital dermatitis) may be looked at as differing from the other types of neurodermatitis chiefly by the importance of estrogenic deficiency in their pathogenesis [7]

Why does neurodermatitis so frequently occur at the suboccipital fossa, and wherein lie the reasons for endocrine implications? Variations in an atopic element, such as specific allergic reactivity, seem incapable of explaining selectivity of site Seborrheic or infectious factors appear not to be the answer External influences seem to have no clear role unless one thinks of heat, perspiration or sebaceous activity, and, if these are localizing factors, they probably are activated by autonomic nervous mechanisms One might hypothesize local differences in ionic metabolism, but these are not yet demonstrated and, if present, should be related either to local anatomic and structural factors (which have not been demonstrated) or, again, to vasomotor or other nervous control Endocrine agents often manifest selectivity of site of action, usually influenced by anatomic structure, but sometimes by way of vasomotor phenomena Psychologic and

7 Lynch, F W Keratoderma Climactericum (Haxthausen), Arch Dermat & Syph **42** 270 (Sept) 1943

could differentiate localized neurodermatitis from disseminated neurodermatitis or from chronic contact dermatitis The extensive reports of Sachs [5] and his associates pointed out differences of degree rather than of kind (and left something to be desired in their unusual classification and use of the term "eczema") Montgomery [6] clearly described the microscopic changes observed in various forms of eczema He expressed the belief that the process in seborrheic dermatitis is not diagnostic and frankly stated that atopic dermatitis or neurodermatitis may not always be distinguished from psoriasis

In dermatitis of the suboccipital fossa I observed the following changes Hyperkeratosis was sometimes present but was neither

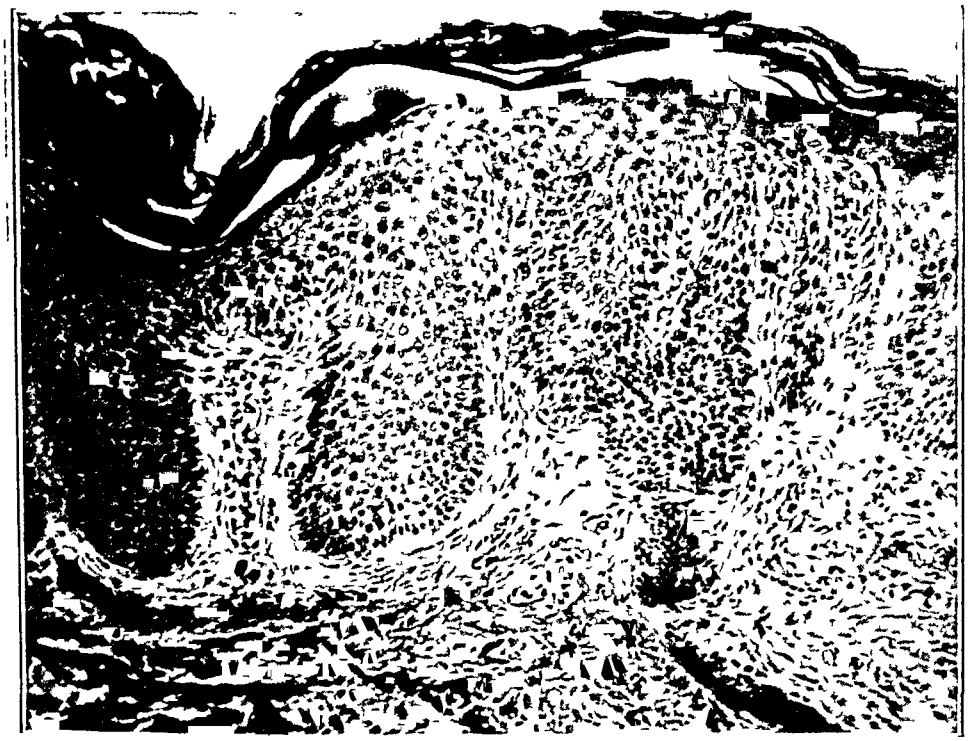


Fig 1—Section from lesion of suboccipital dermatitis, showing characteristic changes There is a moderate amount of hyperkeratosis and parakeratosis, with acanthosis and clubbing of the rete pegs Intracellular edema is accompanied with a few lymphocytes in the epithelial tissues above the papillae Changes in the cutis are less extensive, though there are some edema and lymphocytic infiltration in the papillae

constant in occurrence nor striking in degree Parakeratosis was present fairly constantly but was not intense and was occasionally localized to small areas The stratum granulosum was usually normal, though sometimes absent in areas showing parakeratosis Acanthosis of moderate degree was rather constantly noted and was often asso-

5 Sachs, W , Miller, C S , and Gray, M B Neurodermatitic Reaction, Arch Dermat & Syph **54** 397 (Oct) 1946

6 Montgomery, H , in Ormsby, O S , and Montgomery, H Diseases of the Skin, ed 6, Philadelphia, Lea & Febiger, 1943, pp 247 and 1201

ASSOCIATION OF PROGRESSIVE (MALIGNANT) EXOPHTHALMOS AND LOCALIZED MYXEDEMA

ARTHUR C CURTIS, M D
EDWARD P CAWLEY, M D
AND
EDGAR B JOHNWICK, M D
ANN ARBOR, MICH

IT IS GENERALLY accepted that localized myxedema occurs in conjunction with toxic diffuse goiter (Graves's disease) and often follows surgical removal of a thyrotoxic gland A parallel situation exists with progressive (malignant) exophthalmos The development, progress and duration of localized myxedema so strikingly simulates the course of progressive exophthalmos that one must accept as tenable the supposition that these two conditions are allied manifestations of the same underlying abnormally

OPHTHALMIC COMPONENT OF TOXIC DIFFUSE GOITER

It is now recognized that there exist both a classic type and a special ophthalmopathic[1] variety of ocular change in association with toxic diffuse goiter Ocular proptosis, an integral part of the syndrome comprising typical toxic diffuse goiter, may progress to a severer and more serious variant known as malignant exophthalmos In most instances this development follows surgical removal of a thyrotoxic gland

Since the demonstration by Loeb and Bassett[2] of an extract with thyrotropic quality from the anterior lobe of the pituitary gland, other extracts have been prepared which, when injected, produce changes similar to those found in the thyroid gland of toxic diffuse goiter, after which development the colloid material disappears, the epithelium becomes hyperplastic, and the alveolar cavities collapse Signs of hyper-

From the Department of Dermatology and Syphilology, University of Michigan Medical School

Read at the Sixty-Eighth Annual Meeting of the American Dermatological Association, Inc, San Diego, Calif, April 26, 1948

This article was accepted for the August issue, a special number dedicated to Dr Udo Julius Wile, but was omitted from that issue for technical reasons

1 Means, J H The Nature of Graves' Disease, with Special Reference to Its Ophthalmic Component, Am J M Sc **207** 1 (Jan) 1944

2 Loeb, L, and Bassett, R B Comparison of Effects of Various Preparations of Anterior Pituitary Gland on Thyroid of Guinea Pig, Proc Soc Exper Biol & Med **27** 490 (March) 1930

infiltrate tended to involve the upper portion of the cutis earlier and more constantly but in later stages might be either perivascular or diffuse in distribution It was not perifollicular

On reviewing the aforementioned changes, one might think that psoriasis could be differentiated rather easily, but study of sections from psoriatic lesions of the scalp showed that in this area one does not constantly observe the changes regarded as characteristic of psoriasis Sections from seborrheic dermatitis showed changes different in degree rather than in essential features, there were perhaps more edema, acanthosis and cellular infiltration In general, the microscopic process can be differentiated from that of contact dermatitis Sections from suboccipital dermatitis show the changes which Sachs spoke of as "the neurodermatitic reaction" and correspond well with Montgomery's description The changes in the connective tissues in this disorder seem to have been greater than those that were mentioned in Sachs's and Montgomery's descriptions

THERAPY

Unfortunately, but not surprisingly, the therapeutic attempts were so varied that one can hardly say what regimen was most satisfactory Topically most patients were asked to try boric acid ointment or a mild (6 to 10 per cent) ammoniated mercury ointment If these were noneffective, 1 per cent of phenol may have been added to the former, or 5 to 10 per cent of ichthammol N F or 1 to 3 per cent of crude coal tar was incorporated in an oxycholesterol-petrolatum ointment base (aquaphor®) or fatty acid esters of diethanolamine with petrolatum (hydrosorb®) or, less frequently, in a soft zinc oxide paste Roentgen radiation was used in most cases (but not if it had been previously given by others), in fractional doses, such as 75 r, beginning with weekly intervals and gradually tapering off, seldom exceeding six to nine treatments Diffuse seborrheic features were treated when present, but this procedure was not emphasized and in some cases was deliberately ignored in order to determine that such treatment is not necessary though it may be helpful

While some patients responded rapidly to simple measures, it seemed that many required attention to general hygienic improvement, such as regularity of hours, avoidance of overwork, adequacy of sleep and avoidance of persons or circumstances having frustrating or otherwise irritating influences, or, less successfully, an attempt was made to change the patient's reactions to such influences As an adjuvant, sedation was frequently prescribed, not as nocturnal hypnosis but in the form of phenobarbital, ½ grain (0 03 Gm), or N-methyl phenobarbital (mebaral®), 1½ grains (0 09 Gm) given twice or three times

mone was shown by the work of Rawson, Sterne and Aub[7] who demonstrated that if the thyroid-stimulating hormone is mixed as a substrate with cultures of thyroid cells it loses its physiologic activity This loss is due to inactivation, since activity can be restored by reducing agents Rawson, Graham and Riddell[8] further showed that thyrotoxic goiter cells inactivate twice as much thyroid-stimulating hormone as do normal thyroid cells In progressive exophthalmos, unheated urine contains large quantities of active thyrotropic hormone In progressive exophthalmos there is a total of active or inactive

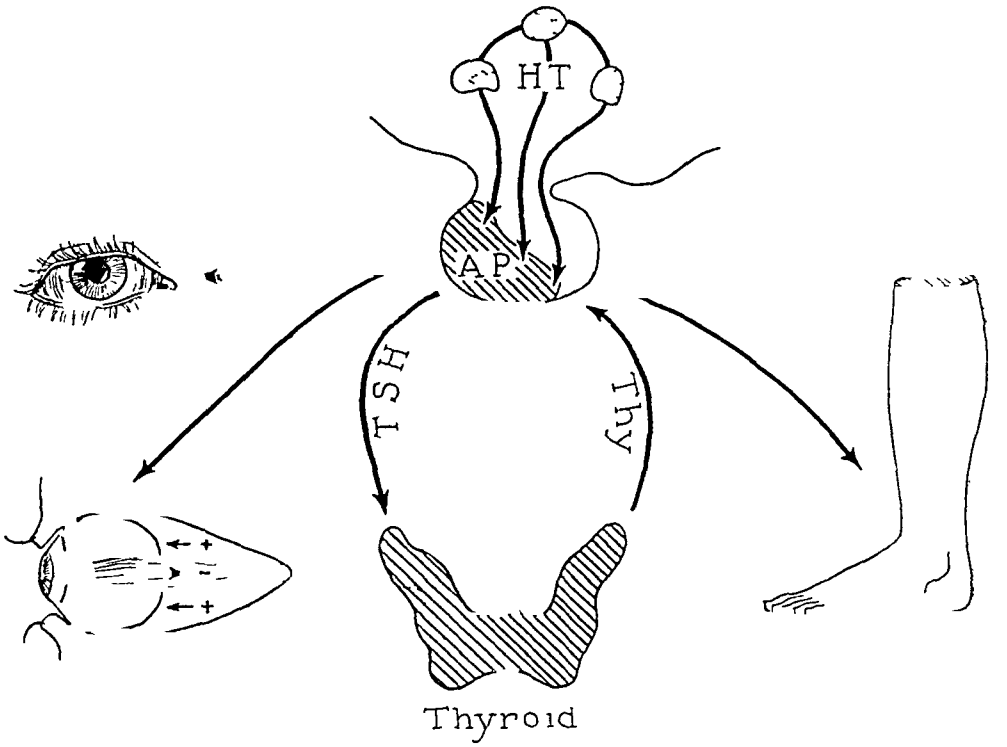


Fig 1—Schematic representation of the pituitary-thyroid axis described by Salter[13] and modified by Means[1] *HT* represents the hypothalamus *AP*, the anterior lobe of the pituitary gland, *TSH*, the thyroid-stimulating hormone and *Thy*, the thyroxin secreted by the thyroid gland cells A normal leg and eye are shown The balance between the push of the retrobulbar contents and the pull of the eye muscles is also illustrated The arrow from *AP* to the thyroid gland to the anterior lobe of the pituitary gland represents normal amounts of the secretion of thyroxin which inhibits secretion by the anterior lobe of the pituitary gland The arrows from *AP* to the eye and leg are to illustrate the effects of the thyroid-stimulating hormone on these normal structures

7 Rawson, R W , Sterne, G D , and Aub, J C Physiological Reactions of Thyroid-Stimulating Hormone of Pituitary Its Inactivation by Exposure to Thyroid Tissue in Vitro, Endocrinology **30** 240 (Feb) 1942

8 Rawson, R W , Graham, R M , and Riddell, C B Physiological Reactions of Thyroid Stimulating Hormone of Pituitary Effect of Normal and Pathological Human Thyroid Tissues on Activity of Thyroid Stimulating Hormone, Ann Int Med **19** 405 (Sept) 1943

justified 1 When menopausal (climacteric) factors were clearly present in the history, two to four months of estrogenic treatment, when added to the more usual remedies, usually led to satisfactory results 2 Persons with unsatisfactory results frequently displayed emotional and psychologic factors related to environmental phenomena which were not easily susceptible of modification

COMMENT

Certain comments may be pertinent in reviewing the results of this survey of 83 patients with dermatitis of the suboccipital region The disorder occurs chiefly in women, at all ages and with about the same frequency as neurodermatitis in general There is perhaps a significant difference in a lower incidence in the group under 20 years of age and a higher incidence in the 30 to 40 year period The relation to atopy seems neither more nor less evident than it is with neurodermatitis at other sites When the condition is compared with other examples of neurodermatitis, the most evident variation is the increased incidence of association with abnormal menstruation The nature of the abnormality cannot be stated with certainty, but it appears to be a diminution in estrogenic activity

Having compared this process with neurodermatitis in general, it is reasonable for one to inquire what evidence is available to link it with that disorder The clinical features are variable within certain limits and cannot be regarded as characteristic of a single form of neurodermatitis, such as lichen chronicus simplex It cannot be assumed that the clinical variations occur only as results of trauma or treatment of a lichenified eruption More often it seems that one is dealing with a more or less moist inflammatory papular eruption It can be distinguished from psoriasis clinically, and sometimes with microscopic aid Contact dermatitis may sometimes be superimposed, but usually this process can be excluded clinically, and in the cases studied the microscopic features were different from those of contact dermatitis Seborrheic factors were not particularly evident in this series of cases and seemed not to be very significant when present The microscopic features in 29 cases were characteristic of neurodermatitis, and it must be concluded that both the clinical and the microscopic features in this series of patients were those to be expected in neurodermatitis

In general, the patients responded rather well to treatment, though it is difficult to develop particular enthusiasm for any single therapeutic regimen In spite of widespread pessimistic views, it appears that good results are common, often regardless of long duration The

thalmos is relatively more frequent in men,[11] there is controversy as to the role of the gonads in its production.[12] The effect of the secretion of each gland on the other has been referred to as the pituitary-thyroid axis.[13]

The changes produced in the orbit by the thyroid-stimulating hormone are an actual increase in volume of the retrobulbar structures, due to edema and cellular infiltration. The weakness of the extrinsic ocular muscles, due to edema and cellular infiltration, and the pressure

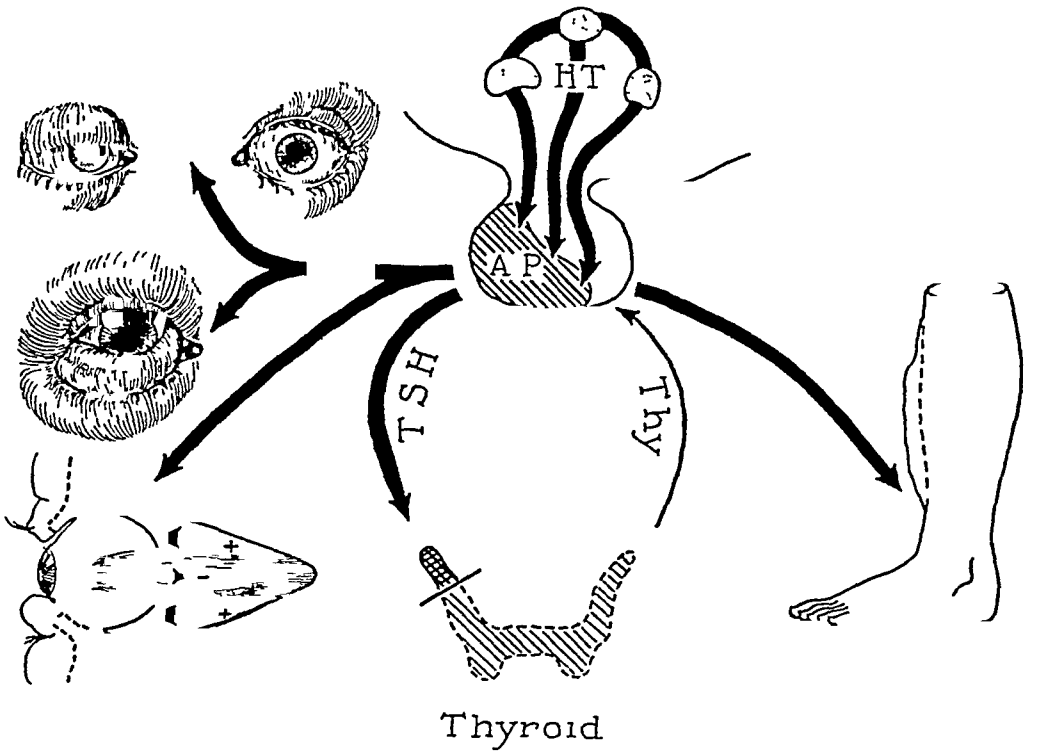


Fig. 3.—Schematic representation of the pituitary-thyroid axis in progressive exophthalmos. The drive of the thyroid-stimulating hormone on other structures as a result of hypothalamic stimulation is now uninhibited because of thyroidectomy or atrophy and consequent decided reduction of the thyroid gland's neutralizing secretion of thyroxin. The eyes show exophthalmos, and the lids are retracted or ptotic. Chemosis is present, and edema of the periorbital tissue is prominent. These signs may be unilateral. Weakness of the rectus and oblique muscles of the eye and of the levatores palpebrarum may be present, and divergent or convergent strabismus may be seen, with or without ptosis. There is hypertrophy of the eye muscles, which become weak, and proptosis is more appreciable as a result of the push of edematous structures behind the eye and the pressure from swollen muscles. Localized edema of the legs is not infrequently present.

11. Marine, D.: Studies on Pathological Physiology of Exophthalmos of Graves' Disease, Ann. Int. Med. **12**: 443 (Oct.) 1938.

12. Dobyns, B. M.: Studies on Exophthalmos Produced by Thyrotropic Hormone. I. A Study of Exophthalmos Produced by Various Thyrotropic Hormones and the Influence of the Testes on the Exophthalmos, Surg., Gynec. & Obst. **82**: 290 (March) 1946.

13. Salter, W. T.: The Endocrine Function of Iodine, Cambridge, Mass., Harvard University Press, 1940.

emotional disturbance often influences the site of disturbed function, probably by use of the autonomic system, but this theory of the mechanism needs much elaboration

CONCLUSION

The analysis of a series of 83 cases of suboccipital dermatitis has provided evidence suggesting that this disease is a form of neurodermatitis, differing from other forms not only in the site involved but also in frequent association with estrogenic abnormality and with psychologic and emotional factors, which may possibly influence the selection of site I am incapable of describing the mechanism involved but can only call attention to the frequency of incidence of nuchal feelings of tension in women at the climacteric, the less known fact that the nuchal region is a zone of erotic significance in certain lower animals, such as the cat, and the well known fact that many incidents which lead to psychologic dissatisfaction are said to give one a "pain in the neck"

1466 Lowry Medical Arts Building (2).

nized, ulceration of the conjunctiva, with subsequent ophthalmitis, has occurred and enucleation has been necessary There is a definite tendency for activity of the process to be self limited to a few months or years, but the exophthalmos seldom completely subsides [1]

LOCALIZED MYXEDEMATOUS COMPONENT OF TOXIC DIFFUSE GOITER

The term localized myxedema is especially incongruous and paradoxic It implies a cutaneous myxedematous disorder fundamentally related to hypothyroidism, despite the fact that most examples have occurred in conjunction with toxic diffuse goiter

Pillsbury and Stokes [20] recorded the case of a woman who had a subtotal thyroidectomy for toxic diffuse goiter She later presented the signs and symptoms of generalized myxedema and was relieved by the ingestion of desiccated thyroid gland After she discontinued medication both generalized myxedema and infiltrated plaques of localized myxedema developed over the tibias Further administration of desiccated thyroid afforded relief from the signs and symptoms of constitutional myxedema but did not alter the status of the pretibial plaques The failure in this case, as well as in others, of long-continued and adequate medication with desiccated thyroid to influence localized myxedema is strong presumptive evidence that this disorder and constitutional myxedema are etiologically unrelated The thyroid-stimulating hormone, which is so closely identified with the cause of progressive exophthalmos, may well be the fundamental factor in production of the lesions of localized myxedema (fig 3)

The microscopic features of localized myxedema are demonstrable in all clinically recognized lesions There are usually edema, homogenization, fraying and splintering of the dermal connective tissue elements Those changes probably precede myxedematous degeneration of the collagen, which eventuates in the presence of variable amounts of mucin in the thickened cutis The latter feature relates localized myxedema pathologically to generalized myxedema The occurrence of stellate cells probably immature connective tissue cells,[20] scattered throughout the mucin has been described, although this is apparently not a consistent observation Flattening of the epidermis and obliteration of the rete ridges, if present, are secondary to the underlying dermal edema Mucin is found microscopically in the dermis in both constitutional and localized myxedema, although in the latter disorder huge quantities of the material are usually apparent when the condition has reached the clinical horizon

The lesions of localized myxedema are roughly oval indurated yellowish brown plaques, occasionally as large and thick as a man's

20 Pillsbury, D M, and Stokes, J H Circumscribed Myxedema of the Skin Arch Dermat & Syph **24** 255 (Aug) 1931

thyroidism, such as increased heart rate, rise in metabolic rate, increased susceptibility to oxygen want, decreased iodine in the gland, increased iodine in the blood and exophthalmos [3] occur It is also known that exophthalmos is not produced by the administration of the thyroid hormone to animals, nor is the gland of toxic diffuse goiter any more toxic when ingested than is a normal gland

Whether the thyroid-stimulating hormone is the same as the exophthalmos hormone seems to have been answered by Albert,[4] who found, after injecting derivatives obtained from the anterior lobe of the pituitary gland of the sheep into the Atlantic minnow, that an exophthalmic factor was present which paralleled the action of the thyrotropic fraction qualitatively and quantitatively, whereas other fractions were ineffective in producing proptosis, even though they were employed in much greater dosage Several investigators [5] showed that exophthalmos, experimentally produced by the administration of thyrotropic hormone, was much severer if the animals had previously been thyroidectomized, these observations upholding the theory that the thyroid-stimulating hormone is the cause of exophthalmos and that ablation of the thyroid gland enhances the effect of the hormone

Friedgood showed that the thyroid gland of guinea pigs responded at first to the thyrotropic hormone by an increased metabolic rate and glandular hyperplasia but later became refractory even though the amount of thyroid-stimulating hormone given was increased During the refractory stage the glandular hyperplasia disappeared and exophthalmos began to appear The proptosis became most prominent during the refractory phase [5b] This refractoriness of the thyroid gland to the thyroid-stimulating hormone was shown by Collip and Anderson to be due to an inhibiting substance (antihormone) which they found in the serum of treated animals [6]

That the secretion of the thyroid gland, probably thyroxin or a thyroxin-like substance, in turn modifies the thyroid-stimulating hor-

3 Best, C H, and Taylor, N B Physiological Basis of Medical Practice, ed 4, Baltimore, Williams & Wilkins Company, 1945, p 726

4 Albert, A The Experimental Production of Exophthalmos in Fundulus by Means of Anterior Pituitary Extracts, Endocrinology **37** 389 (Dec) 1945

5 (*a*) Marine, D, and Rosen, S H Exophthalmos in Thyroidectomized Guinea Pigs by Thyrotropic Substance of Anterior Pituitary and Mechanism Involved, Proc Soc Exper Biol & Med **30** 901 (April) 1933 (*b*) Friedgood, H B Experimental Exophthalmos and Hyperthyroidism in Guinea Pigs Clinical Course and Pathology, Bull Johns Hopkins Hosp **54** 48 (Jan) 1934 (*c*) Smelser, G K Experimental Production of Exophthalmos Resembling That Found in Graves' Disease, Proc Soc Exper Biol & Med **35** 128 (Oct) 1936

6 Collip, J B, and Anderson, E M Production of Serum Inhibitory to Thyrotropic Hormone, Lancet **1**·76 (Jan 13) 1934

which the thyroid gland cannot liberate enough thyroxin to inactivate this secretion (fig 3)

The thyroid-stimulating hormone is known to be a potent factor in the formation of edema Its antagonist, thyroxin, possesses diuretic and dehydrating properties The edema-producing quality of active thyroid-stimulating hormone no doubt contributes much to the evolution of progressive exophthalmos It may have the same effect in initiating localized myxedema

It has been recognized that the lesions of localized myxedema may increase in size after thyroidectomy This development is analogous in those patients with ophthalmopathic toxic diffuse goiter to the progression of exophthalmos following thyroidectomy Collagen, from which mucin is derived,[24] is not present in the orbital contents in appreciable quantity, though it occurs abundantly in the skin This fact probably accounts for the occasional huge deposits of mucin in localized myxedema and its apparent absence in the orbits of progressive exophthalmos, despite an otherwise seemingly close relationship

The clinical course pursued by both localized myxedema and progressive exophthalmos is practically identical The onset may be simultaneous Both appear most often after thyroidectomy for toxic diffuse goiter Both persist for months or years, but activity is definitely self limited Spontaneous regression, inconstant and unpredictable, has been observed with each disorder That such a phenomenon occurs suggests a refractory state, then a recession of lesions in man similar to that noted by Friedgood in animals,[5b] possibly due to the formation of an antihormone, such as that suggested by Collip and Anderson,[6] which neutralizes the thyroid-stimulating hormone

Plummer and Wilder,[24a] in a symposium on exophthalmos fourteen years ago, made the following observations, which anticipated in some measure the correlation of progressive exophthalmos and localized myxedema

> Why should the external rectus muscles become swollen and hardened, and enlarge to several times their normal thickness? Why should edema develop in the lids when it was absent in the stage featured by a high basal metabolic rate? The evidence from the laboratory suggests that overfunction of the anterior lobe of the pituitary body may play a part in the production of this abnormality
> The edematous contents of the orbit are comparable in some respects to localized subcutaneous areas of mucinous edema, which are found in rare cases of exophthalmic goiter, particularly after thyroidectomy

The administration of thyroid extract is not often productive of notable results with either progressive exophthalmos or localized

24 MacLeod, J M H, and Muende, I Practical Handbook of the Pathology of the Skin, ed 3, New York, Paul B Hoeber, Inc, 1946

24a Plummer, W A, and Wilder, R M Etiology of Exophthalmos Constitutional Factors, with Particular Reference to Exophthalmic Goiter, Tr Am Acad Ophth **39** 41, 1934

thyroid-stimulating hormone greater than that in the urine of a person with a normal gland [9] Rawson concluded that in toxic diffuse goiter the pituitary gland overacts in regard to the secretion of thyroid-stimulating hormone In toxic diffuse goiter thyroid-stimulating hormone is inactivated, but in ophthalmopathic toxic diffuse goiter either a large proportion of the thyroid cells have been surgically removed or they cannot rise to the stimulus, and hence most of the thyroid-stimulating hormone remains active Depression of activity of

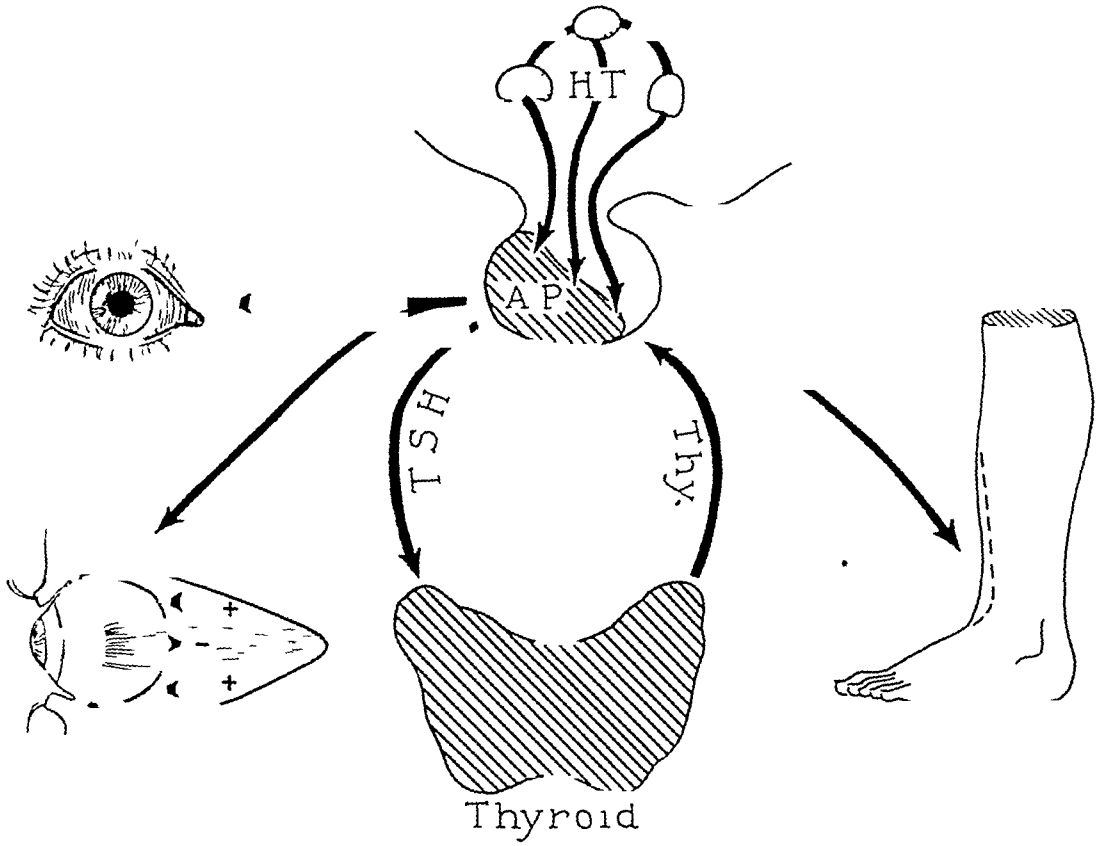


Fig 2—The pituitary-thyroid axis now shows increased activity of the whole system due to toxic diffuse goiter, with hyperplasia of the thyroid gland, exophthalmos and edema of the leg It is believed that the stimulus which starts the cycle of increased secretion arises from shock, worry, responsibility or previous illness, for example, in an already susceptible person [1] The hypothalamus increases its stimulus to the pituitary gland. This action causes increased thyroid-stimulating hormone to be secreted, which secreting in turn causes thyroid glandular hyperplasia and edema, hypertrophy of the muscle and retraction of the lids of the eye, these developments producing exophthalmos Edema of the leg occurs The thyroid gland secretes more thyroxin in an attempt to neutralize the thyroid-stimulating hormone The balance now is at higher or accelerated level

the thyroid-stimulating hormone in rat pituitary secretion to less than 5 per cent of normal by administration of thyroid was shown by Purves and Griesbach [10] Although it was pointed out that progressive exoph-

9 Rawson, R W Personal communication to the author, cited by Means [1]

10 Purves, H D, and Griesbach, W E Effect of Thyroid Administration on Thyrotropic Activity of Rat Pituitary, Endocrinology **39** 274 (Oct) 1946

for three weeks, at the end of which time the basal metabolic rate was +2 per cent, and a subtotal thyroidectomy was performed Microscopic examination of the thyroid gland showed pathologic changes of toxic diffuse goiter The patient's convalescence was uneventful, and she was discharged on May 3, 1941

The patient returned to the hospital on June 24, 1941, and stated that she felt much improved subjectively Exophthalmometer readings, however, were 29 mm for the right eye and 29 mm for the left eye, and the ophthalmologist diagnosed progressive exophthalmos Her basal metabolic rate was —2 per cent At about this time the department of gynecology performed a dilation, curettage and conization of the cervix because of cystic cervicitis and polypoid glandular erosion of the cervix The examining physician noted "an area of brawny induration on the medial aspect of the left shin" but did not have the patient seen by a dermatologist Because of further progression of the exophthalmos, intracranial decompression of the orbits was advised and subsequently performed by the neurosurgeon in two stages between July 1 and July 15 Pathologic examination of orbital



Fig 4—*A* (case 6), showing ptosis of both lids, more pronounced on the right, and muscular palsy The photograph was taken in 1948, thirteen years after the onset of toxic diffuse goiter and two and one-half years after a third subtotal thyroidectomy *B* (case 3), showing pronounced exophthalmos on the left side and swelling of the periorbital tissues Exophthalmos is decided but deceiving because there is no retraction of the lid *C* (case 4), illustrating to good advantage the widened palpebral fissure and exposure of the sclera of the eye above the iris *D* (case 1), showing severe conjunctival chemosis, often an early manifestation of progressive exophthalmos *E*, the widened palpebral fissure and muscle palsy of progressive exophthalmos *F*, unilateral lid ptosis and exophthalmos and edema of periorbital tissues, more evident on the left side

muscle showed variation in staining of the muscle fibers and heavy lymphocytic infiltration (fig 5 *A* and *B*) Special staining procedures carried out at a later date revealed that one of two specimens of muscle contained mucin in small quantities

The patient was not seen again until December 1946, at which time she was examined only by the ophthalmologist, who noted that she had been feeling well and that her exophthalmos had definitely regressed without medication during the interim but that there was weakness of the internal rectus of the right eye and lid lag of the left eye Exophthalmometer readings were 19 25 mm for the right

exerted by the swollen retrobulbar contents lead to anterior displacement of the globe [14] An actual increase in muscle fat has also been demonstrated [15] and may likewise be of some importance Administration of the thyroid-stimulating hormone to animals produces alterations in cardiac and skeletal muscle fibers [16] closely akin to those found in the corresponding muscles of human beings with toxic diffuse goiter, which observation may account in some measure for the myasthenia associated with toxic diffuse goiter [17] Figures 1, 2 and 3 graphically illustrate the pituitary-thyroid relationship

The clinical picture of progressive exophthalmos is an extremely variable one Means [18] emphasized that classic exophthalmos may later become progressive and stated the belief that such severe subsequent changes should probably be regarded as a continuous process rather than a special type of toxic diffuse goiter The staring facies and widening of the palpebral fissure, with exposure of the sclera of the eye above the iris, are pathognomonic of toxic diffuse goiter In progressive exophthalmos, bulging of the lids, chèmosis of the conjunctiva, muscle weakness and palsies and limitation of ocular movements (especially those upward), as well as exophthalmos, are characteristic Such changes are not infrequently unilateral The onset of progressive exophthalmos may on occasion be abrupt, though more often it is gradual On rare occasions the ocular disorder becomes so pronounced that orbital decompression becomes necessary [19] In rare cases, in which the implications of severe and progressive exophthalmos have not been promptly recog-

14 (*a*) Moore, R F Exophthalmos and Limitation of Eye Movements of Graves' Disease, Lancet **2** 701 (Oct 2) 1920 (*b*) Thomson, E S Orbital Edema in Exophthalmic Goiter, Am J Ophth **7** 27 (Jan) 1924 (*c*) Smelser, G K Histology of Orbital and Other Fat Tissue Deposits in Animals with Experimentally Produced Exophthalmos, Am J Path **15** 341 (May) 1939 (*d*) Paulson, D L Experimental Ophthalmos and Muscle Degeneration Induced by Thyrotropic Hormone, Proc Staff Meet, Mayo Clin **14** 828 (Dec 27) 1939 (*e*) Maimini, C G Exophthalmometric Measurements in Patients with Thyroid Diseases with Some Discussion of Their Significance, Ann Int Med **16** 415 (March) 1942

15 Paulson [14d] Maimini [14e]

16 Dobyns, B M Studies on Exophthalmos Produced by Thyrotropic Hormone II Changes Induced in Various Tissues and Organs (Including the Orbit) by Thyrotropic Hormone and Their Relationship to Exophthalmos, Surg, Gynec & Obst **82** 609 (May) 1946, III Further Study of Changes Induced in Fat by Thyrotropic Hormone (Tissue Reactions Associated with Exophthalmos), ibid **82** 717 (June) 1946

17 Footnote deleted

18 Means, J H Hyperophthalmopathic Graves' Disease, Ann Int Med **23** 779 (Nov) 1945

19 Naffziger, H C Progressive Exophthalmos Following Thyroidectomy Its Pathology and Treatment Tr Am S A **49** 168, 1931

hyperthyroidism with typical symptoms Her basal metabolic rate at that time was said to have been + 56 per cent Thyrotoxic symptoms were completely relieved, and the patient felt unusually well until April 1945, when she first noticed bilateral painless swelling of the lids, proptosis and diplopia, which persisted Her past health, except as noted, had always been excellent

Examination at the time of admission disclosed bilateral ocular proptosis, with exophthalmometer readings of 15 mm for the right eye and 21 mm for the left eye, with limitation of abduction in the left eye At this time the basal metabolic rate was + 10 per cent There were no other significant findings The patient was placed on 15 drops of strong iodine solution and 1½ grains (0 09 Gm) of desiccated thyroid a day When she returned in one month the basal metabolic rate was + 4 per cent and the exophthalmometer readings 18 mm for the right eye and 23 mm for the left eye Despite cessation of treatment with the strong iodine solution and an increase in the dose of thyroid extract to 4 grains (0 26 Gm) each day, which subsequently had to be reduced to 3 grains because of thyrotoxic symptoms, there was continued progression of the exophthalmos Readings on March 21, 1946, were 22 mm for the right eye and 24 mm for the left eye, with appreciable paresis of the left inferior oblique muscle and weakness in abduction of the left eye (fig 4*B*) The basal metabolic rate at this time was plus 30 per cent The endocrinologist advised roentgen irradiation of the pituitary gland, but the patient did not return for further observation or treatment

Case 4—B F, a white woman aged 35, was admitted as an outpatient to the ophthalmology service of the University Hospital on Feb 14, 1945 In March 1942 she had had symptoms of hyperthyroidism and slight exophthalmos, with a basal metabolic rate of + 59 per cent A thyroidectomy was done elsewhere in April 1942, after which the patient was relieved of most of her symptoms but did not notice any change in the proptosis The basal metabolic rate in December 1942 was + 36 per cent Because of recurrent symptoms of hyperthyroidism, another thyroidectomy was performed in November 1944, at which time the basal metabolic rate was + 4 per cent, and the exophthalmos subsequently became much worse

Physical examination at the time of admission showed pronounced bilateral conjunctival hyperemia and chemosis over the lower half of each globe and palpable fusiform enlargement of the extraocular muscles (fig 4*C*) There were no other significant findings The basal metabolic rate was — 6 per cent Despite continued administration of dessicated thyroid in adequate dosage, the exophthalmos was progressive, and in August 1945 the basal metabolic rate was + 5 per cent, and the exophthalmometer readings, 32 mm for each eye At about this time the patient decided to go elsewhere for further observation and treatment

Case 5—R Y, a white man aged 45, was admitted to the medical service of the University Hospital on Feb 18, 1935, complaining of intolerance to heat, nervousness, irritability, incresaed appetite and loss of 16 pounds (7 3 Kg) which had been sustained since the onset of symptoms in December 1934 The patient's health in the past had been good

The examining physician found that the thyroid gland was palpable only at the isthmus and noted that this was deep in the suprasternal notch There was slight cardiac enlargement, with a gallop rhythm heard best at the apex, and the blood pressure was 170 systolic and 90 diastolic The rest of the physical examination showed normal conditions

Complete laboratory studies revealed a basal metabolic rate of + 45 per cent, which two days later was plus 40 per cent, but no other significant findings A diagnosis of toxic diffuse goiter was made and the patient placed on treatment

hand, which do not pit on pressure and seldom exceed three or four Their surface has at times the appearance of pigskin and is less often studded with dome-shaped papules Mild itching and burning of the involved skin are sometimes present Such lesions are usually bilateral and limited to the lower anterolateral surface of the legs Nodular infiltrations occurring on the face, arms, back and scrotum have been described in the literature under the same title [21] Many patients with localized myxedema confined to the legs have had antecedent and transient pitting edema of the lower extremities This, however, is not an infrequent accompaniment of toxic diffuse goiter [1] Systemic treatment has little or no appreciable effect on the lesions of localized myxedema They may show evidence of spontaneous regression after a few months or years, thus paralleling the usual career of progressive exophthalmos In at least 1 case the plaques were surgically removed for cosmetic reasons

PROGRESSIVE EXOPHTHALMOS AND LOCALIZED MYXEDEMA AS ALLIED MANIFESTATIONS OF THE SAME UNDERLYING DISORDER

Progressive exophthalmos is not frequently encountered, and localized myxedema is a dermatologic rarity, yet we have been able to find 5 recorded examples in which patients had the two disorders simultaneously [22] In 1 of these, reported by Netherton,[22c] the localized myxedema cleared after cauterization of the anterior lobe of the pituitary gland [23] Other reports have implied, in title or otherwise, coexistence of the two diseases but have devoted their discussion exclusively to one or the other component It seems probable that if all patients with progressive exophthalmos were examined for localized myxedema, or the reverse, an ever increasing number of persons who had these disorders concurrently would be observed

In a majority of cases, toxic diffuse goiter, with one or more subsequent thyroidectomies, precedes the development of either progressive exophthalmos or localized myxedema Occasional exceptions to this rule may be explained by a lack of hyperplasia of the thyroid gland or its rapid atrophy The former may be due to an inability of the thyroid gland to respond to the thyroid-stimulating hormone, and the latter, to exhaustion The pituitary-thyroid axis is then altered either by the surgical removal of the thyroid gland, with a resultant excess of unneutralized thyroid-stimulating hormone or by the situation in

21 (*a*) Pillsbury and Stokes [20] (*b*) O'Leary, P A Localized Solid Edema of the Extremities in Association with Exophthalmic Goiter, Arch Dermat & Syph **21** 57 (Jan) 1930

22 (*a*) Pillsbury and Stokes [20] (*b*) Ingram, J T Circumscribed Myxedema Associated with Hyperthyroidism, Brit J Dermat **45** 19 (Jan) 1933 (*c*) Netherton, E W Localized Myxedema Case Presentation, Arch Dermat & Syph **48** 123 (July) 1943

23 Netherton, E W Personal communication to the authors

was a cerebrovascular accident, although permission for an autopsy could not be obtained The exophthalmos was still pronounced, but the localized myxedema had regressed considerably, there still being some evidence of the disorder on the left shin

CASE 6—D S, a white man aged 34, was admitted to the surgical service of the University Hospital on Oct 23, 1945, complaining of recurrent enlargement of the thyroid gland In 1935, he had had symptoms of severe hyperthyroidism, including exophthalmos After subtotal thyroidectomy elsewhere, there had been considerable improvement for six months, after which time the symptoms recurred and a second operation was performed, with further removal of thyroid tissue The patient subsequently felt well for several years, and the exophthalmos partially regressed In the spring of 1943 the patient noticed a nodule in the center of the thyroidectomy scar, together with symptoms of recurrent hyperthyroidism, including nervousness, ease of fatigue, palpitation, increased sweating and tremor of the hands At about the same time he became aware of a small, flesh-colored papule, which was asymptomatic, on the anterior aspect of the right leg During the next year and a half the patient's symptoms became severer and the lesion on the right leg increased in size and was accompanied with a similar one on the left shin The patient's health in the past, except as noted previously, had always been good

Physical examination at the time of admission revealed a large mass of thyroid tissue palpable above the old operative scar in the midline There were appreciable bilateral exophthalmos, with exophthalmometer readings of 23 mm for the right eye and 25 mm for the left eye, and ptosis of both upper lids, more pronounced on the right On the anterior aspect of each leg, extending from the ankle to within 6 inches (15 cm) of the knee, were indurated yellowish brown plaques, the surface of each being studded with numerous papules and small nodules The rest of the physical examination showed normal conditions

Complete laboratory studies revealed a basal metabolic rate of — 15 per cent but no other significant findings The endocrinologist made a diagnosis of thyrotropic exophthalmos and suggested the possibility of neoplastic change in a thyroid adenoma, while the dermatologic consultant described the lesions on the legs as those of localized myxedema A third subtotal thyroidectomy was performed in November 1945 The pathologist reported adenocarcinoma of the thyroid gland, while microscopic examination of tissue from the lesion on the leg showed pronounced mucinous degeneration and edema of the corium, a picture interpreted as that of localized myxedema High voltage roentgen therapy was administered to the thyroid region postoperatively

Exophthalmometer readings on December 13 were 24 mm for the right eye and 27 mm for the left eye The patient was discharged and advised by the endocrinologist to take 1½ grains of desiccated thyroid each day in an effort to avert further progression of an already severe exophthalmos He returned to the hospital in April 1946, at which time his basal metabolic rate was —11 per cent and he had gained considerable weight and was feeling well During subsequent months he continued the ingestion of thyroid extract and complained only of tiring easily In July 1946, his basal metabolic rate was —7 per cent and in August 1947 —4 per cent When examined most recently at the hospital on Feb 20, 1948, the patient stated that he had felt better for the preceding few months than for the past several years He had found that best results were obtained from 3 grains of thyroid extract each day The exophthalmos had regressed considerably, but the ptosis was more decided (fig 4*A*) and the lesions of localized myxedema were somewhat smaller (fig 6*B*) There was no demonstrable recurrence of the thyroid carcinoma

myxedema Its apparent benefit in some cases may have been due to spontaneous improvement Thiouracil, which interferes with the synthesis of thyroxin by the thyroid gland, produces what has been aptly termed a medical thyroidectomy Because the thyroid-stimulating hormone factor is not only uninhibited but may increase as a response to the failure of function of the thyroid gland, medication with thiouracil has not proved effective and may be harmful Irradiation of the pituitary gland in toxic diffuse goiter holds some promise [25]

In patients with toxic diffuse goiter and ophthalmic changes suggestive of progression, thyroidectomy should be avoided Because these patients may also acquire localized myxedema, the same contraindication for operation should hold for the two conditions

REPORT OF CASES

Case 1—C C, a white man aged 50, was admitted to the ophthalmology service at the University Hospital, Aug 7, 1947, complaining of bleeding on urination, as well as protrusion of the eyes His ocular difficulties had begun in June 1947 with photophobia and conjunctivitis, which had become severer His past health had always been good except as noted previously

Physical examination showed bilateral eversion of the inferior bulbar and palpebral conjunctivas, with extreme chemosis, decided protrusion of the globes (fig 4 *D*) and exophthalmometer readings of 25 mm for the right eye and 27 mm for the left eye The patient was referred to the department of urology and found to have a carcinoma of the urinary bladder, for which a successful radical operation was subsequently performed

Laboratory studies revealed a basal metabolic rate of —2 per cent and plasma cholesterol, 126 mg per hundred cubic centimeters A diagnosis of progressive exophthalmos was made, and the patient started the ingestion of 1 grain (0 06 Gm) of thyroid extract each day Numerous subsequent examinations showed the basal metabolic rate to be consistently in the neighborhood of —2 per cent. There was slow improvement of the progressive exophthalmos, for the exophthalmometer reading in March 1948 was 17 mm for each eye The patient had continued the ingestion of thyroid, although the amount had not been consistent, varying from 1 to 3 grains (0 19 Gm) each day

Case 2—L S, a white woman aged 52, was admitted to the surgical service of the University Hospital on April 4, 1941 She had been as well as was usual until July 1940, when she had first noticed slight protrusion of her eyes, photophobia, myasthenia, intolerance to heat and loss of weight During subsequent months these manifestations had become more pronounced, and at the time of admission she had lost 40 pounds (18 1 Kg) Her past health otherwise had been good

Significant ocular findings were bilateral exophthalmos, with exophthalmometer readings of 23 5 mm for the right eye and 25 mm for the left eye and some lid lag The thyroid gland was palpable and firm but not nodular The skin was moist and warm, and the examining physician made a diagnosis of exophthalmic goiter Significant laboratory findings were a basal metabolic rate of +49 per cent and plasma cholesterol of 194 mg per hundred cubic centimeters The patient received strong iodine solution U S P (Lugol's solution) by mouth

25 Thompson, W O What's New in Endocrinology, J A M A **136** 314 (Jan 31) 1948

treatment in several of the other cases were equivocal This observation would appear to be corroborative experimental evidence that thyroxin inactivates thyrotropin All three examples of localized myxedema occurred after surgical removal of the thyroid gland The patient in case 6 had three thyroidectomies but acquired progressive exophthalmos and localized myxedema after the second operation

The numerous recorded determinations of basal metabolic rate do not reveal convincing metabolic evidence of hyperthyroidism or hypothyroidism at the time the localized myxedema or progressive exophthalmos developed, although toxic diffuse goiter preceded its onset in most instances Neither are the plasma cholesterol levels definitely indicative, although those recorded, with one exception, were somewhat lower than normal

A microscopic review of the pathologic material obtained from the orbits of several persons with progressive exophthalmos revealed edema of the muscles and retrobulbar fat, with an increase in muscle fat in some cases There was round cell infiltration of variable degree in almost every case, and not infrequently this was concentrated in the vicinity of blood vessels Degenerative muscular changes encountered included variation in staining power, loss of cross striations and areas of hyalinization and fragmentation Special staining reactions revealed small quantities of mucin in 1 instance (case 2), this observation providing further evidence of the relations between localized myxedema and progressive exophthalmos It was seldom possible to find all features fully developed in one specimen

The microscopic examination of tissue from both patients with localized myxedema showed the characteristic microscopic features of this process

In general, a careful review of the cases presented here lends support to the hypothesis that localized myxedema and progressive exophthalmos are probably allied manifestations of the same underlying disorder

SUMMARY

1 Progressive exophthalmos, a severer and more serious variant of the ocular proptosis which is part of the syndrome comprising typical toxic diffuse goiter, develops in most instances after surgical removal of a toxic thyroid gland Abundant experimental evidence has been presented within recent years to show that a thyroid-stimulating hormone elaborated by the anterior lobe of the pituitary gland is a major factor in the production of progressive exophthalmos

2 Similarly, the lesions of localized myxedema, usually bilateral and limited to the lower anterolateral surface of the legs, are almost always associated with or preceded by clinical manifestations of toxic diffuse goiter, and thyroidectomy or thiouracil therapy usually initiates their onset

eye and 24 5 mm for the left eye There was no further notation about the lesion on the leg, which may well have been localized myxedema

CASE 3—H F, a white woman aged 41, was admitted as an outpatient to the ophthalmology service of the University Hospital on Oct 22, 1945 Four years previously she had undergone a thyroidectomy elsewhere because of

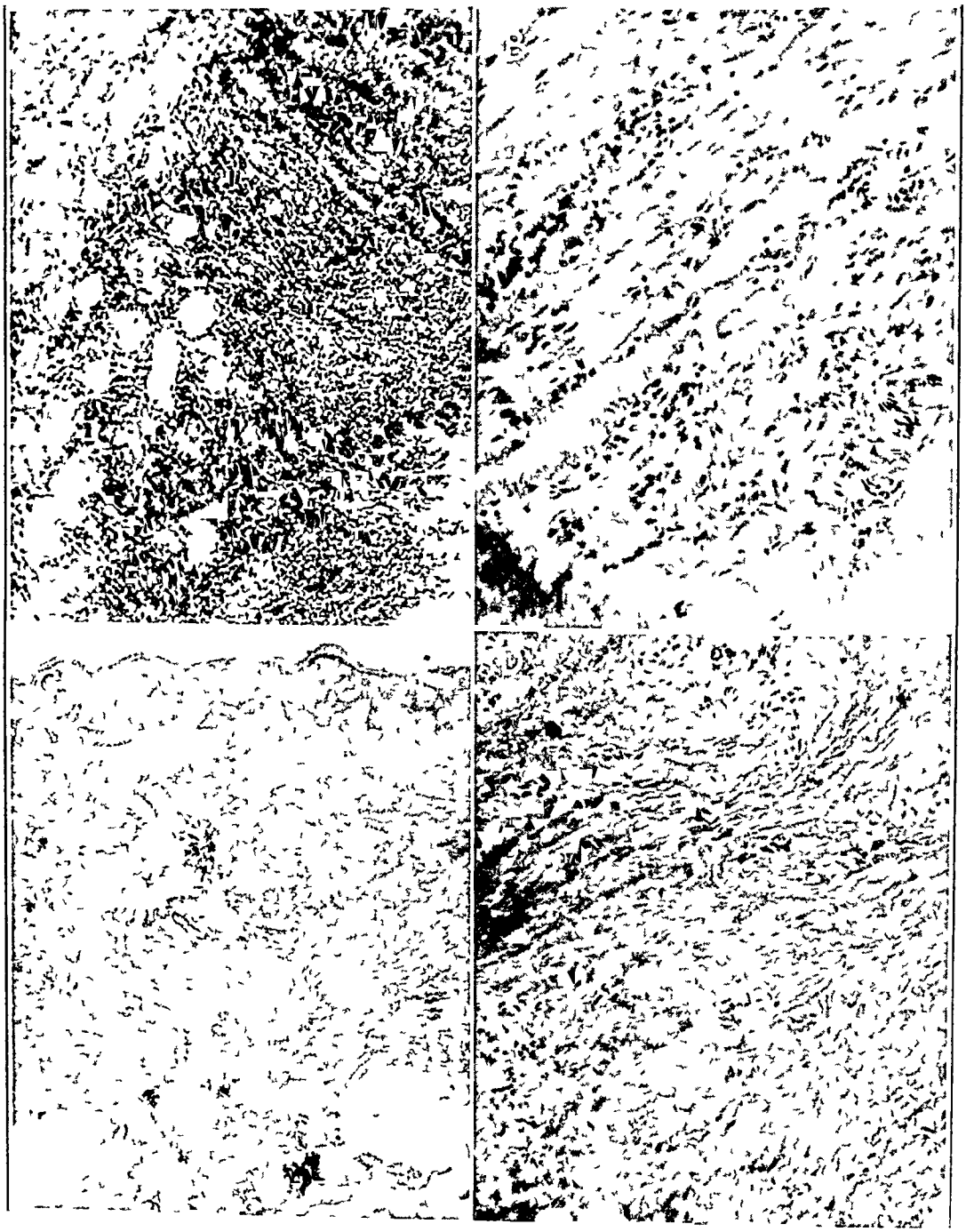


FIG 5—*A*, high power view of orbital muscle obtained at operation in case 2 showing the heavy lymphocytic infiltration which obscures the muscle bundles in most areas *B*, high power view of another section of orbital muscle from the patient in case 2 A lymphocytic infiltrate is apparent, although it is not as pronounced as in *A* There is also some edema *C*, low power view of a microscopic section from one of the lesions of localized myxedema in case 5 Large quantities of mucin are present in the dermis The microscopic features of the lesions of the leg in case 6 were almost identical *D*, high power view of the mucin observed in case 5 A few sweat gland tubules can be seen

and the proptosis regressed Obviously, such a radical procedure is contraindicated in the treatment of localized myxedema Although recorded cases identical with this are not numerous, the observation in itself lends strong support to Dr Curtis' hypothesis

It is unfortunate that there is no simple and safe procedure for inhibition of hyperfunction of endocrine glands other than the thyroid The mechanism in the production of localized myxedema and the reason for the predilection of the condition for the pretibial areas remain to be determined Dr Curtis suggested that the edema-producing quality of the thyroid-stimulating hormone, which probably contributes to the evolution of progressive exophthalmos, likewise initiates localized myxedema Recently Watson has shown that the skin in pretibial myxedema contains an excess of hyaluronic acid, and he has expressed the opinion that the myxedema is related to disturbance of the hyaluronic acid–hyaluronidase balance Further investigation may show that hormones influence the action of cutaneous enzymes which are active in the metabolism of mucopolysaccharides present in the interfibrillar substance of collagen tissue

We are indebted to Dr Curtis for emphasizing the association of progressive exophthalmos and localized myxedema and for pointing out their parallel clinical course I concur in his hypothesis that they are allied manifestations of toxic diffuse goiter

Dr Martin F Engman Jr, St Louis I should like to ask Dr Curtis to say something about the factor of heredity

Dr Paul A O'Leary, Rochester, Minn I was intrigued by Dr Curtis' conception of localized myxedema because of my interest in this condition for many years In a paper I presented on this subject in 1930, I purposely avoided the use of the term localized myxedema because the late Dr Henry Plummer objected strenuously to the concept that myxedema and hyperthyroidism in the form of toxic diffuse goiter could occur in the same patient at the same time Practically all the patients in the early cases we studied who presented plaques of solid edema of the extremities had recently gone through an episode of hyperthyroidism of the toxic diffuse goiter type, and some were experiencing a second episode following a postoperative remission It was my feeling at that time that this complication was seen most frequently in those persons who had had severe edema of their lower extremities as a result of myocardial disease secondary to the hyperthyroidism

Since then I have seen several patients with localized plaques of solid edema, with histologic evidence of myxedema, in whom clinical, laboratory and historical evidence was lacking for hyperthyroidism, either past or present Likewise exophthalmos was not present in all our patients who manifested these plaques

For this reason the work of Meyer, followed by that of Watson and Pierce, as mentioned by Dr Netherton, advanced an interesting concept, namely, that mucin was precipitated in the skin and elsewhere as a result of a disturbance in the hyaluronidase balance—possibly the result of an interference in the counter-reaction function of a theoretic enzyme Although prepared to do so my associates and I have not as yet had the opportunity, because of lack of case material, to apply the suggestions of these investigators

One other point is that in all the cases we have been able to follow the plaques eventually disappear spontaneously, occasionally in four to five years, even though some of the patients retain evidence of hyperthyroidism

Dr Herman Sharlit, New York I too have been interested in this report by Dr Curtis It should be taken into consideration in explaining the

with strong iodine solution, which had to be discontinued after three weeks because of his intolerance to the medication

On March 12, 1935, the basal metabolic rate was reported as + 28 per cent, and two days later a subtotal thyroidectomy was performed The pathologist reported the tissue as that of iodized toxic diffuse goiter After an uneventful convalescence the patient was discharged on March 25 In May 1936 he returned, stating that he had felt much improved after the operation but that he had recently noticed some protrusion of his eyes, as well as thickened areas on the lower portion of the legs The ophthalmologist reported bilateral exophthalmos with slight lid lag and exophthalmometer readings of 22 mm for each eye On the anterior surface of each shin was a large, tawny, indurated plaque which extended to the lateral surface of the leg (fig 6*A*) and had the clinical features



Fig 6—*A* (case 5), the large plaque of localized myxedema on the lower right leg, shown to good advantage There was a similar lesion on the left leg *B*, the localized myxedema of case 6, five years after it had first appeared There had been very considerable regression of the lesions during this period

of localized myxedema The basal metabolic rate was + 3 per cent, and the plasma cholesterol, 127 mg per hundred cubic centimeters Two years later, in April 1938, the patient returned to the hospital having had no treatment during the interim Exophthalmometer readings were 23 mm for the right eye and 23 5 mm for the left eye, and there was persistence of the previously noted lid lag as well as slight limitation of abduction The basal metabolic rate was + 6 per cent Microscopic examination of a biopsy specimen from the lesion on the leg showed the epidermis to be atrophic, overlying a corium in which there was almost complete mucinous degeneration of the connective tissue elements (fig 5*C* and *D*)

The patient was not seen again for eight years, after which time he returned to the hospital and died within forty-eight hours, having had what apparently

PROMIN® IN THE TREATMENT OF CERTAIN DERMATOSES

L G BEINHAUER, M D
AND
F M JACOB, M D
PITTSBURGH

THE therapeutic effects of promin® (sodium p,p'-diaminodiphenylsulfone-N,N'-didextrose sulfonate) were studied in a group of common dermatoses Senior members of the staff of the Department of Dermatology of the University of Pittsburgh School of Medicine participated in the study, and their independent observations were used as a basis for this report

A total of 81 patients were treated with the drug for periods ranging from two weeks to twenty-seven months The patients were arbitrarily divided into two groups The first group consisted of 33 patients (table 1), whose disease was primarily of the chronic type, which had failed to respond to previous therapy In the second group there were 48 patients (table 2) whose diseases were the more acute forms of dermatoses Promin® was administered orally against all diseases except scleroderma, against which intravenous therapy was used The oral administration consisted of a daily dosage of 0 8 to 1 8 Gm of the drug and was continued over treatment periods of four weeks to twenty-seven months Intravenous therapy was given daily in dosage of 2 5 to 5 Gm for two weeks, then 5 Gm weekly over a period of four months The oral administration of 1 8 Gm daily could be continued only for a relatively short period (ten to fourteen days) whereas a smaller dosage of 0 8 to 1 2 Gm was tolerated longer (two to twenty-seven months) The regimen of treatment was not interrupted unless toxic symptoms appeared

Promin® jelly (5 per cent of the agent in a tragacanth base) was used as a local application in all instances Prior to treatment physical examinations of the patients were made, including a blood count and urinalysis Patients were examined biweekly for the first month, then weekly as long as treatment was continued Urinalyses and red and

From the Department of Dermatology, University of Pittsburgh School of Medicine

This article was accepted for the August issue, a special number dedicated to Dr Udo Julius Wile, but was omitted from that issue for technical reasons

Dr E A Sharp, director of clinical investigation, Parke, Davis & Company, Detroit, supplied the promin®

COMMENT

The belief that progressive exophthalmos and localized myxedema are coexistent far oftener than recorded is supported by the fact that 3 of 4 patients recently seen at the University Hospital have had both The fourth patient had only localized myxedema Cases 5 and 6 are examples of such association Five cases records of localized myxedema found in the literature mentioned the concurrent existence of progressive exophthalmos as an incidental finding [22] Dr Frank C Hoak and Dr Eugene Hand have each presented a similar case [26] If these are added to the 3 we have observed, a total of 8 patients are known to have had both

The staring facies and widely retracted lids make the exophthalmos of toxic diffuse goiter strikingly apparent If retraction of the lid disappears or is replaced by ptosis, or if chemosis occurs, the exophthalmos seems less severe, and yet the degree of exophthalmos may actually be as great or greater This is illustrated by comparing the photographs of the patients in cases 4 and 1 (fig 4 *C* and 4 *D*) Exophthalmos is more apparent and seems greater in the former than the latter patient, and yet exophthalmometer readings at the time the photographs were taken showed essentially the same degree of exophthalmos in the two

Case 6 (fig 4 *A*) illustrates bilateral ptosis, edema and, on close inspection, muscle weakness The patient shown in figure 4 *F* had pronounced exophthalmos, obscured, however, by ptosis and periorbital edema The unilateral character of the disorder is rather striking in in this instance Figure 4 *E* shows evidence of palsy of the muscle to good advantage, while figure 4 *B* (case 3) illustrates the distended, discolored, periorbital tissues, a condition unilateral in this instance but which may be either unilateral or bilateral A typical tawny plaque of localized myxedema in the usual location is shown in figure 6 *A* (case 5), while figure 6 *B* (case 6) illustrates the nodular, yet circumscribed, character of the lesions of the leg It seems probable that one or the other component, usually localized myxedema, because of its location and innocuous character, is often unrecognized or minimized Case 2 is a likely example

With one exception, the cases presented here illustrate the importance of thyroidectomy in the development of progressive exophthalmos It is worth noting that in case 1, in which progressive exophthalmos made its appearance without benefit of antecedent thyroidectomy, the response to medication with thyroid extract was good, while the results of similar

26 A patient with localized myxedema and hyperthyroidism presented by Dr Frank C Hoak at the Buffalo meeting of the Central States Dermatological Association, April 10, 1948, had progressive exophthalmos as well Both phenomena appeared six months after the patient started medication with thiouracil A few days later, Dr Eugene Hand, of Saginaw, Mich, sent us photographs of one of his patients who exhibited both disorders after thyroidectomy for toxic diffuse goiter

drug, and no permanent sequelae were encountered A routine of discontinuing treatment for one week after three weeks of treatment resulted in fewer and milder reactions and allowed us to continue treatment in 2 instances for periods of eighteen to twenty-seven months without incident Only 5 patients disclaimed toxic reactions, and these belonged to the second group The local use of promin® jelly produced contact dermatitis in 2 patients

REPORT OF CASES

The results from the use of promin® orally, parenterally and locally were not encouraging Of the 81 patients treated, 10 were improved and 71 were unimproved The local use of promin® jelly had no specific curvative effect Four cases warrant mention

CASE 1.—A woman aged 27 had patches of discoid lupus erythematosus for three years With promin® therapy complete healing occurred in four weeks, but due to the appearance of a persistent bluish tint of the face, further treatment was refused A recurrence began within three weeks after withdrawal of the drug

CASE 2.—A man aged 52 had ulcerative lesions of lupus erythematosus of the lips of five years' duration, these promptly healed within two weeks after the initiation of treatment Recurrence developed ten days after withdrawal of the drug, which caused nausea and severe headaches Alternating periods of one week of treatment and one week without treatment resulted in complete healing, which was maintained over a period of six months

CASE 3.—A man aged 51 had chronic discoid lupus erythematosus of twenty-seven years' duration, which healed within eight weeks and remained healed over a treatment period of twenty-one months on a daily dosage of 1 5 Gm of promin®

CASE 4.—A woman aged 32 had a generalized scleroderma of three years' duration, associated with ulcerative sclerodactylia which began four months prior to treatment with the drug The ulcerative lesions then healed within one month Treatment was continued during the latter half of a pregnancy, which terminated normally at full time Discernible changes were not observed in pathologic examination of biopsy specimens taken at intervals of six months

SUMMARY AND CONCLUSION

The use of promin® (sodium p,p'-diaminodiphenylsulfone-N,N'-didextrose sulfonate) in the treatment of a group of common dermatoses was disappointing Toxic reactions were common Therapy with this drug offers no advantage over the recognized treatment regimens against the group of dermatoses studied

5026 Jenkins Arcade

7026 Jenkins Arcade

3 The development, progress and duration of localized myxedema so strikingly simulates the course of progressive exophthalmos that one must accept as tenable the supposition that the two conditions are allied manifestations of the same underlying disorder and probably both due to an excess of thyroid-stimulating hormone

4 The association of both progressive exophthalmos and localized myxedema in 3 of the 4 cases we have studied and in 7 other reported or known cases is further evidence that these two disorders are clinically related

University Hospital

ABSTRACT OF DISCUSSION

DR EARL W NETHERTON, Cleveland We are indebted to Drs Curtis, Cawley and Johnwick for this excellent paper After a careful consideration of accumulated experimental and clinical data, Dr Curtis and his collaborators have proposed the hypothesis that progressive exophthalmos and localized myxedema are allied manifestations of the same underlying pathologic condition, toxic diffuse goiter I was unaware of the sparsity of recorded cases demonstrating this association

A recent review of 13 cases of localized myxedema seen at the Cleveland Clinic showed that all the patients had had thyroidectomy for toxic diffuse goiter prior to the appearance of the localized myxedema There was a record of an associated exophthalmos in 7 cases Three patients had severe progressive exophthalmos With a Cleveland colleague, I recently observed a patient in whom progressive exophthalmos and localized myxedema appeared during the treatment of toxic diffuse goiter with thiouracil A surgical thyroidectomy had not preceded medical treatment Thus there are 3 additional unrecorded cases of toxic diffuse goiter in which the progressive exophthalmos and localized myxedema developed concurrently Exophthalmos has been observed in toxic diffuse goiter more often than has localized myxedema It is probable that mild cutaneous changes have been overlooked in cases of progressive exophthalmos Furthermore, histologic sections of pretibial skin from patients with progressive exophtalmos and with absence of clinical localized myxedema might show foci of myxedematous degeneration, which may not become recognizable clinically Dr Curtis' hypothesis suggests that this investigation is indicated

The diagrammatic presentation of the concept of the thyropituitary axis clearly explains some of the perplexing features of localized myxedema, particularly its development in toxic diffuse goiter after the administration of thiouracil or after thyroidectomy Furthermore, the presentation also explains the failure of localized myxedema to disappear after the administration of thyroxin and thyroid extract

If the concept of the thyropituitary axis is correct, and since it has not been determined that additional and more complex hormone relationships may be of etiologic importance in toxic diffuse goiter and in progressive exophthalmos and localized myxedema in particular, the logical therapeutic approach should be directed toward decreasing the production of the thyrotropic hormone Roentgen ray treatment of the pituitary gland has been helpful in some cases of progressive exophthalmos Dr Curtis has referred to a patient with severe progressive exophthalmos and localized myxedema, whose case I presented at a meeting of the Cleveland Dermatological Society In this patient, because of severe exophthalmos, the left orbit was decompressed and the anterior lobe of the pituitary gland was cauterized After this procedure the localized myxedema disappeared

The scarcity of Jews with gonorrhea in this study was striking Berkowitsch [3] found the gonorrhea rate the same in Jews and in gentiles Physicians at this hospital who had worked in the venereal clinics of New York city informed me that gonorrhea was common in Jews but more prevalent in gentiles It is likely that some Jews went to their private physicians for treatment of gonorrhea, particularly at the time when venereal disease carried with it the penalty of misconduct with loss of pay

Syphilis In 1855 Jonathan Hutchinson [4] first made the observation that syphilis was uncommon in Jews This was confirmed by Feldman [5] in a study at the venereal clinics of Metropolitan Hospital in 1882, where syphilis was found to be four times more common in gentiles Polduan,[6] in a study of the vital statistics of New York city, found syphilis to be three times more prevalent in gentiles Circumcision, being almost universal in Jews, was considered to be the reason for this situation Brietenstein,[1] in a study of 15,000 circumcised African soldiers and 18,000 European soldiers, many of whom were uncircumcised, found venereal disease, including syphilis, to be commoner in the uncircumcised Lloyd and Lloyd,[2] at Guy's Hospital, concluded that circumcision was not an important factor in acquisition of syphilis, but they did not compare their percentages of circumcised and uncircumcised with those observed in groups that had no history of venereal disease

The 532 cases of syphilis in this series were in 344 gentiles, 4 Jews and 184 Negroes, of these, 22 2 per cent of the gentiles, 17 5 per cent of the Negroes and all the Jews were circumcised The paucity of Jews in this group could be due to the same reason as that suggested in the discussion of the group with gonorrhea Syphilis certainly was less common in circumcised gentiles and Negroes This observation becomes even more striking when these cases are subdivided into the following groups 358 cases with primary syphilis on the distal end of the penis, where the presence or absence of the prepuce could affect the acquisition of syphilis, 88 cases with the primary sore on the middle or upper portion of the shaft or some other part of the body with secondary lesions, and 86 cases with no history of primary or secondary sores

3 Berkowitsch, M E Ostasiat Rundschau **3** 19, 1928

4 Hutchinson, J M Times & Gaz **11** 542, 1855

5 Feldman, W M The Jewish Child, New York, Bloch Publishing Company, 1918, p 213

6 Polduan, C, and Weiner, L New England J Med **208** 407, 1933

background for localized infiltration of mucin that physicians frequently see these conditions locally, particularly in the legs, with no apparent clinical evidence of glandular deficiency Recently my associates and I treated at least 2 patients with hyaluronidase enzymes, and the reaction was immediate and spectacular It may be that, in studying this enzyme and the hyaluronic acid reaction, investigators are getting more to fundamentals behind the infiltration of mucin by taking a larger picture It may be that there is more than one mechanism that results in the production of mucin

DR FRED D WEIDMAN, Philadelphia I should like to ask Dr Curtis whether there is evidence that mucinoid degeneration occurs in the involuntary muscles The skin is the particular field of us present, and I am wondering whether we can pick up early evidence of this dystrophy in a simple histologic examination of the skin Time and time again I have felt that the muscles appeared far too broad and edematous in proportion to the development of the hair follicle Would this material in the involuntary muscles be mucin? The mucin in myxedema is a different kind of mucin from that observed in epithelial structures, it has a definite chemical reaction It will not reduce Fehling's solution without preliminary hydrolysis Perhaps we may learn something in examination of the skin that will bear no relation to the mucinoid degeneration in the involuntary muscles, whether it is connected with hyperthyroidism or not I recommend that in future studies of diseases of this kind the condition of the arrectores pilorum be inquired into

DR ARTHUR C CURTIS, Ann Arbor, Mich I wish to thank the discussers for their interesting and constructive ideas Dr Netherton asked why localized myxedema appeared on the legs I neither know why nor whether this occurrence has anything to do with dependency of the extremities I agree with Dr Netherton that patients who have progressive exophthalmos often have cutaneous lesions which are overlooked In one of our patients with malignant exophthalmos (case 2), lesions on the shins, which from their description were probably localized myxedema, were present

The role of the pituitary gland in toxic diffuse goiter was shown by Means,[18] who reported the case of identical twin girls, 1 of whom acquired round worm infection The passage of these worms was so shocking to the child that she acquired toxic diffuse goiter That the pituitary gland was involved in the case of this adolescent girl is shown by the fact that after having the disease she grew 1½ inches taller than her twin Fourteen years ago Plummer and Wilder[17] speculated on the possible association of progressive exophthalmos and localized myxedema and suggested tentatively that they might be due to the same factor and both related to an overfunction of the anterior lobe of the pituitary gland

Dr O'Leary used the term solid edema in his excellent article on this subject[21b] Solid edema is a better term than localized myxedema

Dr Sharlit mentioned cases of localized mucinous infiltration without apparent evidence of glandular deficiency I have not seen such cases, nor have I had any experience with determination of the presence of hyaluronic acid in these diseases, but I think these points provide a fertile field for future endeavor

Dr. Weidman mentioned the possibility of mucinous degeneration in the arrectores pilorum In toxic diffuse goiter the smooth muscles do show change, but I have not observed mucinous degeneration in the smooth muscles of the skin because I have not looked for it I shall investigate this problem further when I return

ized circumcision during the acute stage, with excellent results, shortening the hospital stay Patients in his series averaged thirty-two days of hospitalization, as compared with the months needed for persons treated with the usual methods advocated at that time

A diagnosis of chancroid was made in the present series in 138 cases, of which 60 were in gentiles and 78 in Negroes, 91 6 per cent of the gentiles and 96 1 per cent of the Negroes were uncircumcised

The chancroid lesions were usually multiple in the uncircumcised persons and in the few circumcised patients were single and cleaner The circumcised persons had quicker healing when treated with sulfonamide compounds than did the uncircumcised The differentiation from chancre and Vincent's balanitis was difficult in the uncircumcised

Lymphogranuloma Venereum The diagnosis of lymphogranuloma venereum was made for 11 patients, of whom 26 were gentiles and 18 Negroes All these persons were uncircumcised

Granuloma Inguinale One case of granuloma inguinale was seen in an uncircumcised white person

The Percentages of Circumcised Persons Among Subjects Without Venereal Disease and Among Those with Various Venereal Diseases

Diagnosis	Jews	Gentiles	Negroes
No venereal disease	99 8%	34 %	42 2%
Gonorrhea	100 %	23 6%	13 %
Syphilis	100 %	22 2%	17 5%
Chancre on distal end of penis	No case	13 9%	12.7%
Chancroid	No case	8 4%	3 9%
Lymphogranuloma venereum	No case	0 %	0 %

NONVENEREAL INFECTIONS

The following interesting observations were made in cases of nonvenereal disease of the penis The diagnosis of Vincent's balanitis was made for 22 patients, all of whom were uncircumcised and 8 of whom had pronounced phimosis Vincent's balanitis often recurs Circumcision is the treatment of choice in that event

Verruca acuminata of the penis was seen in 61 persons, of whom 40 were gentiles and 21, Negroes All but 2 of these were uncircumcised One case of perianal verruca acuminata was seen in a Jew Verruca acuminata is uncommon in the circumcised, and prior to therapy with resin of podophyllum the treatment of choice was circumcision Circumcision still is valuable in recurrent cases

Nonspecific balanitis was not seen in the circumcised

Herpes progenitalis was seen in this study in about the same proportion in circumcised and uncircumcised patients with venereal dis-

white blood cell counts were performed for each patient every two weeks The toxic reactions which were encountered are worthy of report One of the most distressing from the point of view of the patient was a peculiar discoloration of the skin, which appeared within eight to forty-eight hours as a peculiar, dusky, slate gray or bluish tint It first appeared about the lips, tip of the nose, cheeks, neck, extremities and body in the order named The intensity varied with the natural pigmentation of the skin and was unmistakable in members of the white race A detectable change in color was discernible in the Negro patient and was most prominent on the sclera and on the oral mucosa The discoloration was not associated with any appreciable numerical reduction of the erythrocytes or hemoglobulin, and in no instance was there any evidence of

TABLE 1—*Results of Promin® Therapy Against Chronic Dermatoses*

Disease	Cases	Improved	Unimproved	Reactions
Chronic discoid lupus erythematosus	14	3	11	14
Chronic disseminated lupus erythematosus	5	2	3	5
Sarcoidosis	3	0	3	3
Erythema induratum	2	0	2	2
Lupus vulgaris	4	0	4	4
Scrofuloderma	2	1	1	2
Scleroderma (diffuse)	3	1	2	3

TABLE 2—*Results of Promin® Therapy Against Acute Forms of Dermatoses*

Disease	Cases	Improved	Unim proved	Reactions
Erythema multiforme	8	2	6	6
Erythema nodosum	4	1	3	3
Acute infectious eczematoid dermatitis	14	0	14	13
Impetigo contagiosa	8	0	8	8
Ecthyma	4	0	4	3
Sycosis vulgaris	4	0	4	4
Furunculosis	4	0	4	4
Acute disseminated lupus erythematosus	2	0	2 (died)	2

cardiorespiratory embarrassment This discoloration did not occur in the patients who received intravenous therapy Headaches, mild and severe, were common, annoying and appeared within forty-eight to seventy-two hours Nausea, vomiting, vertigo, myalgia, insomnia, urticaria and malaise were encountered Dyspnea, palpitation, hematuria and albuminuria were absent A numerical reduction in the number of erythrocytes and hemoglobulin was observed in 9 patients and appeared within six to eight weeks Leukopenia, peculiar to lupus erythematosus, was not generally affected as a rule However, in 5 patients a definite elevation of the leukocyte count was maintained by the administration of the drug and was accompanied with definite clinical improvement Recticulocytosis occurred on three occasions and appeared several days after the observation of a numerical reduction of the erythrocytes All reactions were controlled by withdrawal of the

gentiles Many Negroes are promiscuous In Negroes there is little circumcision, little knowledge or fear of venereal disease and promiscuity in almost a hornet's nest of infection Thus the venereal rate in Negroes has remained high

Between these two extremes there is the gentile, with a venereal disease rate higher than that of Jews but much lower than that of Negroes

CONCLUSIONS

Gonorrhea and syphilis are less common in the circumcised

Chancroid is rare in the circumcised

Lymphogranuloma venereum is almost never seen in the circumcised

211 Bearinger Building

CIRCUMCISION AND VENEREAL DISEASE

EUGENE A HAND, M D
SAGINAW, MICH

THERE has been little written from a statistical standpoint to confirm or deny the popular medical belief that the circumcised are less prone to contract venereal disease This paper will present a statistical study of the incidence of circumcision in a group free from venereal disease as compared with that of groups with various forms of venereal disease, to determine the influence of circumcision on venereal disease

The material for this study was obtained during 1945 from the venereal clinics of the United States Naval Hospital at St Albans, N Y.

NO VENEREAL DISEASE

From a group of 790 gentiles, 525 Jews and 76 Negroes who had never had venereal disease it was found that 34 per cent of the gentiles, almost all the Jews and 42 2 per cent of the Negroes were circumcised. The 1 uncircumcised Jew was unorthodox and proud of his prepuce It was difficult to find many Negroes of military age without a venereal history

VENEREAL DISEASE

Gonorrhea Of 522 gentiles, 16 Jews and 511 Negroes who gave a history of gonorrhea, 23 6 per cent of the gentiles, 100 per cent of the Jews and 13 per cent of the Negroes were circumcised The percentage of circumcised gentiles and Negroes was definitely lower in the group with gonorrhea than in the group that never had had venereal infection Brietenstein [1] also found this true, as did Lloyd and Lloyd,[2] who found that 27 6 per cent of the gentiles with gonorrhea had been circumcised, an observation almost identical with that in this study

This article was accepted for the August issue, a special number dedicated to Dr Udo Julius Wile, but was omitted from that issue for technical reasons

Read before the Section on Dermatology and Syphilology at the Ninety-Sixth Annual Session of the American Medical Association, Atlantic City, N J, June 12, 1947

1 Brietenstein, cited by Bloch, I The Sexual Life of Our Time, in Its Relation to Modern Civilization, translated from the 6th German edition by M E Paul, London, Rebman, Ltd, 1908, p 376

2 Lloyd, V E, and Lloyd, N L Brit. M J **1**:144, 1934

Manual epilation, or epilation with the aid of forceps, was probably first used by the Arabs, who constructed the finest brass instruments for this purpose, comparing favorably with the most modern epilation forceps Bazin [1] and his followers revived epilation as a method of treatment for tinea capitis Besnier devoted one morning weekly to the clinical study and teaching of this form of therapy Its steady application for about a century resulted in perfection of technic and the development of many experts in the art of epilation As enthusiasm for this procedure once again waned, it was kept up chiefly by individual advocates, each with his own favorite technic Thus, Hebra [2] proceeded by "holding the hairs indiscriminately and in thin tufts between a blunt edged instrument, a tongue spatula, for instance, and the opposed thumb, and then drawing them out With slight traction the diseased hairs come out, the healthy ones remaining in the follicles" When manual epilation once again returned to favor, it was chiefly accomplished with forceps, but the dosage and duration of such treatment remained completely arbitrary

During the many centuries that have elapsed since manual epilation came into vogue, almost innumerable methods of treatment for tinea capitis have been suggested, tested and abandoned It is remarkable that epilation, though occasionally relegated to the background or temporarily abandoned, has always been restored to favor, and, finally, with the discovery of roentgenotherapy as a means of epilation has become the treatment par excellence for tinea capitis Moreover, cure by roentgen epilation cannot be assured without the adjunct of manual epilation

This fact and the possibility that some of the therapeutic results claimed for the newer fungicides and other agents may be attributable to the manual epilation described as an adjunct, rather than to the various local applications per se, have been mentioned by various writers [3] As previously emphasized, the dosage and duration of manual epilation prescribed have varied with the individual author Some physicians instruct their patients to pull out infected hairs daily [3c] Some epilate twice weekly in the office [3e]

2 Hebra, F On Diseases of the Skin, translated by C H Fagge, London, 1866-1868

3 (*a*) Hartzell, M B Diseases of the Skin, ed 1, Philadelphia, J B Lippincott Company, 1917 (*b*) Steves, R J, and Lynch, F W Ringworm of the Scalp, J A M A **133** 306-309 (Feb 1) 1947 (*c*) Miller, J L, Lowenfish, F P, and Beattie, G F Local Treatment of Tinea Capitis, ibid **132** 67-70 (Sept 14) 1946 (*d*) Schwartz, L Progress in Fungous Disease Therapy, Journal-Lancet **67** 56-59 (Feb) 1947 (*e*) Peck, S M Suggested Methods for the Control of the Present Epidemic of Tinea of the Scalp, Pennsylvania M J **50** 569-573 (March) 1947 (*f*) Lewis, G M, and Hopper, M E An Introduction to Medical Mycology, ed 2, Chicago, The Year Book Publishers, Inc, 1943

The 358 persons with primary syphilis on the distal end of the penis included 216 gentiles and 142 Negroes, of these 13 9 per cent of the gentiles and 12 7 per cent of the Negroes were circumcised

The 88 with primary syphilis not on the distal end or with secondary lesions included 72 gentiles, 2 Jews and 14 Negroes, 47 3 per cent of the gentiles, 29 per cent of the Negroes and all the Jews were circumcised at the time of their infection Though there is a slight difference between the figures given for this subgroup and those for persons without venereal infection, attention is called to the decidedly increased percentage of circumcised in it when compared with the aforementioned group of the persons with primary sores on the distal end of the penis

The 86 who gave no history of primary or secondary lesions consisted of 56 gentiles, 2 Jews, and 28 Negroes, 21 4 per cent of the gentiles, 35 7 per cent of the Negroes and all the Jews were circumcised Here again the percentage of circumcised is higher than in the group with primary lesions on the distal end of the penis In both groups of those without primary sores on the distal end, 36 per cent of the gentiles and 33 per cent of the Negroes were circumcised, a figure which is almost identical with that given for the group free from venereal disease

The diagnosis of syphilis was usually made earlier and with less difficulty, with a better clinical result, in the circumcised This situation existed because many of the uncircumcised were phimotic from birth or had inflammatory phimosis develop as a result of the induration and edema associated with the chancre, this development making the retraction of the foreskin impossible, a result which made the dark field examination difficult The presence of Vincent's organisms under the phimosis also confused the diagnosis The primary sores were usually single in the circumcised and multiple in the uncircumcised

Ulcus mixté, or chancroid infection combined with chancre was much commoner in the uncircumcised Generally the chancres healed more quickly in the circumcised

CHANCROID

Chancroid Berkowitsch found chancroid six times more frequent in gentiles than in Jews Lloyd and Lloyd [2] found that 90 per cent of the patients in their series were uncircumcised In the days prior to the use of sulfonamide drugs, when chancroid infection, particularly the type with buboes, required long hospitalization, Rauschkolb [7] util-

7 Rauschkolb, J E Circumcision in Treatment of Chancroidal Lesions of Male Genitalia Further Observations, Arch Dermat. & Syph **39** 319 (Feb) 1939

epilation can be accomplished accurately and thoroughly with this aid The filter, which is composed of glass with barium silicate and nickel oxide components, permits transmission of only certain wavelengths, and under this light the diseased hairs take on a bright, pale green color, described variously as luminous yellowish green or bright bluish green

The present study includes the results of observation of 104 cases of tinea capitis due to the Microsporum audouini [6] Cases of tinea due to other organisms were excluded, since such infections are usually associated with inflammation, which aids spontaneous cure and therefore complicates the interpretation of results Moreover, it is M audouini which is responsible for the most chronic and epidemic forms of the disease In 16 of these 104 cases, as a reaction some form of kerion developed during treatment, and they were therefore excluded from the series, leaving 88 cases for the study Because of the need for long-continued study of the patients, it was decided to give them all some form of local treatment, in order to insure a more successful period of observation This local treatment consisted in application of an ointment [7] containing 5 per cent undecylenic acid, 3 per cent triethanolamine U S P , 20 per cent zinc undecylenate, 3 per cent sodium tetradecyl sulfate (sodium-2-methyl-7-ethylundecyl sulfate-4), 10 per cent propylene glycol N F (racemic 1-2-dihydroxy-propane), 10 per cent propyl alcohol and 49 per cent carbowax 1500® (a mixture of polyethylene glycols having an average molecular weight of about 550)

The cases were divided into three groups, in the first, which served as the control group, no manual epilation was carried out and only the ointment was used In the second group, manual epilation of the scalp hairs was carried out for approximately one minute, every two weeks In the third group, manual epilation was carried out for five minutes, every two weeks I performed all the epilation

TECHNIC

The following routine was carried out on all patients

1 The heads were shaved once weekly, the morning after examination

2 The heads were shampooed with castile soap once weekly

3 The ointment was rubbed into the affected areas three times a day for five minutes at a time

4 A tight-fitting cap with a paper lining was worn by the patient, this lining was changed once daily and the discarded one burned

5 The patients were asked to return every two weeks for follow-up examination, at which time they were all examined under the Wood filter light

6 Forty-eight cultures were made by Dr Dorothy Spring, Department of Health Laboratories, Pennsylvania Department of Health

7 This ointment was supplied by Wallace & Tiernan Products, Inc, Belleville, N J

ease as in the group without venereal disease This observation should mitigate against the popular treatment of this troublesome condition by circumcision

COMMENT

Venereal infection is less likely in the circumcised because of the physical and histologic changes that occur on the distal end of the penis after circumcision The skin of the glans, corona, frenulum and inner portion of the prepuce in the uncircumcised is more like mucous membrane, being soft, moist and easily traumatized during love play and coitus, with resulting microscopic and macroscopic tears The skin of the corona, glans, frenulum and distal portion of the shaft in the circumcised is tough, keratinized, dry and a degree or more cooler than is the area under the prepuce of the uncircumcised The prepuce, especially when it is phimotic, acts as a sheath holding bacteria acquired during coitus in an excellent moist, warm culture medium, making infection likely through the tears mentioned The opposite is true of the dry, cool, tough skin of the circumcised

Another less important reason for circumcised persons' being less prone to acquire venereal disease is that circumcision is usually commoner in those from better educational, financial and cultural backgrounds This situation gives these persons at least a better chance of proper education regarding sex Their chances of meeting, associating with and cohabiting, in or out of the marital status, with those women least likely to be infected are somewhat better than are those of the uncircumcised Proper sex education would give them at least knowledge of the existence of venereal disease and of how it is contracted It also would provide them with some knowledge of the signs and symptoms, so that, if infected, they seek medical advice early and thus are less likely to infect others of their class

Through the ages, Jews have universally been circumcised on the eighth day after birth This procedure has given them protection against venereal disease even when they have been exposed Though they may be promiscuous in their own race, Jews certainly are less promiscuous than Negroes When infected they tend to seek medical advice early Thus venereal disease has not been introduced into the Jewish race generation after generation Instead the rate has remained the same or decreased, so that the chance of Jews' being infected has decreased

Circumcision is not common among Negroes When done it often is later in life and frequently is due to recurrent venereal disease The sex education of most Negroes is meager They tend to accept venereal disease with less fear or social taboo than do most Jews and

ABSTRACT OF DISCUSSION

DR W A SHOWMAN, Tulsa, Okla Manual epilation in treatment of tinea capitis due to M audouini has received considerable attention in the past few years and Dr Wilson has furnished additional evidence that this infection can be treated successfully by this method It is interesting to note from his report that the total number of cures in those cases in which epilation was carried out in addition to topical application was much higher, yet the extension of the time factor in the epilating process did not shorten the total number of days that was required to obtain a cure It is obvious that the total number of infected hairs removed per unit of time depends a great deal on the operator, and the longer the duration of the epilation procedure, the shorter the total treatment period should be, a supposition which is not substantiated by the report, since it required an average of 185 5 days for group 3 and an average of 171 5 days for group 2 Complete epilation is the most important factor

I agree with the author that forced regulation for the care of infected patients is imperative, but any stipulated time factor for the epilation is not essential, provided that a careful and thorough epilation be performed Pillsbury (Scully J P , Livingood, C S , and Pillsbury, D M The Local Treatment of Tinea Capitis Due to M audouini, *J Invest Dermat* **10** 111 [March] 1948) stated that 90 per cent of cures may be expected with compulsory and supervised treatment They insisted that careful epilation of all fluorescent hairs be performed in conjunction with topical application Since the introduction of the purple X® Bulb (Dennie, C C , and Morgan, D Use of the Purple X bulb in Diagnosis of Fungous Diseases of the Scalp, ARCH DERMAT & SYPH **55** 396 [March] 1947), a more careful manual epilation can be done in the home

Fortunately, those of us practicing in Oklahoma have not had to contend with an epidemic of tinea capitis due to M audouini during the past five years, as revealed by a questionnaire from seven dermatologists reporting from the state A total of 550 cases of all types of tinea capitis were reported from private practice for the past five years From the physicians reporting who furnished culture identification of the causative organism, an incidence of 4 8 per cent due to M audouini was obtained Six of the seven reporting dermatologists resorted exclusively to manual epilation in conjunction with topical treatment One physician reported that in 15 cases epilation by irradiation was used

I am in accord with Dr Wilson that manual epilation in conjunction with topical treatment will effect cure in a high percentage of cases of tinea capitis, though infection with M audouini has not been a major problem in my area

DR LOUIS SCHWARTZ, Bethesda, Md I agree with Dr Wilson that manual epilation shortens the time required to cure tinea capitis Manual epilation removes infected hairs and enables the fungicide applied to the scalp to penetrate the empty infected follicles more easily and kill the fungi lodged there It has certain advantages over roentgen epilation Only infected hairs are removed and disposed of immediately There is no danger of permanent alopecia, and no expert technic is required

The method of treatment used by Dr Wilson was similar to that used by the United States Public Health Service at Hagerstown, Md , Elkhardt, Ind , and several smaller places where there were epidemics of tinea capitis and where from 90 to 100 per cent of cures were obtained among a total of about 1,500 cases

The important differences between Dr Wilson's method and the method used by the Public Health Service are that with the latter epilation of the children in the schools was performed daily under a Wood light and that trained attendants

MANUAL EPILATION IN TREATMENT OF TINEA CAPITIS

JOHN F WILSON, M D
PHILADELPHIA

SINCE manual epilation has played such an important role in the treatment of tinea capitis throughout the ages, and is still recommended by most authorities as an adjunct to the newer drug therapies and fungicides, and even as an indispensable adjunct to curative roentgen epilation, a more precise evaluation of its exact therapeutic significance might lead to progress in the management of tinea capitis, most particularly in the control of epidemics of this disease

A study, therefore, was made of the results of treatment in three groups of cases, in one, serving as the control group, local application of a fungicidal ointment was the only therapy used, and in two this local therapy was supplemented by manual epilation of shorter and longer duration The results obtained will be described in detail, as a preliminary step toward the demonstration of the actual part played by manual epilation, per se or in combined treatments, for the cure of tinea capitis

As early as the third century B C, Heliodorus [1] recommended the application of a skull cap made of pitch plaster for removal of hairs in tinea capitis, the true cause of which was, of course, unknown at that time The warmed pitch was spread on linen and applied to the scalp, and, after being permitted to cool and harden, this cap was removed by a sudden wrench, carrying the hairs with it Although this method was later abandoned as being too barbarous, Sabouraud [1] stated that, properly applied, it was far from being as painful as described, and that he found this method in use in some French provinces as late as the beginning of the twentieth century After the substitution of less painful, but apparently likewise less efficient, methods, physicians of that period reported a higher incidence of the disease in hospitals, where its spread was particularly difficult to control, and where the pitch cap had proved of real help

From the Department of Dermatology, Jefferson Medical College, and the Department of Dermatology, Misericordia Hospital

Read before the Section on Dermatology and Syphilology at the Ninety-Seventh Annual Session of the American Medical Association, Chicago, June 23, 1948

1 Sabouraud, R Du role de l'epilation a la pince en dermatologie, Presse med **39**.113-115, 1931

DR H V ALLINGTON, Oakland, Calif My associates and I agree with Dr Wilson's recommendation of manual epilation and local medication in the treatment of tinea capitis We have in our laboratory a technician trained to teach the parents the technic of manual epilation She demonstrates to them the fluorescence of the hairs and the localization of the areas of involvement on the scalp in natural illumination and under the Wood light and, finally, under the purple X® globe. We do not insist that the parents purchase a purple X® globe but we recommend it

The actual demonstration in the office with the purple X® globe proves, first of all, that the hairs in the case at hand will fluoresce with this source of light, second, it shows the parents what they should see It has been said that the purple X® globe causes satisfactory fluorescence in only about 50 per cent of cases However, in our office, the purple X® globe is satisfactory in a somewhat higher percentage of cases

There are lights available which are designed primarily to show fluorescence in minerals One of these is on display here at the convention These are not generally to be recommended for showing fluorescence in infected hairs, they apparently have a wavelength which is not suitable for this purpose

We instruct the parents to spend whatever time they can each day at home plucking infected hairs If the patient and his parents are cooperative, it is usually possible to achieve a cure in a large percentage of cases within a relatively short time If, however, the patient is uncooperative and the parents are timid and ineffectual, it is usually evident within a short time that treatment with manual epilation and local medication will be a tedious process The method of attack can then be shifted and roentgen epilation resorted to

DR. WILILAM L DOBES, Atlanta, Ga During the past two years, in Atlanta, there has been an epidemic of tinea capitis due to M audouini It was impractical to use roentgen epilation on all clinic patients, and too many private patients refused this procedure because of fear of after-effects It was necessary, therefore, to resort to local treatment The newer fungicides, especially salicylanilid,® were found effective in about 60 per cent of the cases, but the treatment persisted for many months When manual epilation was added, the improvement was more rapid and the percentage of cures higher, but the procedure in most cases was painful to and trying for the patient, as well as for the parent Many refused this treatment

The majority of microsporum infections tend to disappear spontaneously at about the time of puberty Hormonal factors were most likely involved The use of estrogenic substance was tried by various investigators, such as Lewis and Hopper, Poth and Kaliski, Yanez and others The results reported varied I have tried the hormone treatment in more than 50 cases of infection with M audouini I doubt whether any patient was actually cured, but I did find that in using a larger dose of estrogens the hair in about 70 per cent of the cases was sufficiently loosened to permit manual epilation without discomfort to the patient In cases in which local treatment and manual epilation are desired, as an adjuvant treatment I use estrogenic substance, which I give to both men and women The use of testosterone with men was found satisfactory in only a small number of cases Results from diethylstilbestrol U S P were not as satisfactory as the estrogenic substance given by injection Soreness of the breasts was a commoner symptom when diethylstilbestrol was used The usual dose of estrogenic substance was 10,000 to 15,000 international units every five to seven days The hair usually

Roentgen irradiation, while the most effective form of therapy, is of value only in experienced hands, and an adequate number of experienced roentgenotherapeutists may not be available, particularly in time of epidemics [3b] Thallium acetate is indicated only in selected cases and is, besides, extremely toxic It has been suggested and experiments have shown that the fatty acids secreted by adult hair may play some part in rendering adults immune to infection by tinea capitis [4] These therapeutic measures are, however, still in the experimental stage The discovery of an agent that would increase the penetration of fungicides might render even manual epilation superfluous

There are, too, cases in which tinea capitis persists in spite of the most arduous manual epilation It has been observed that a few hairs may continue to fluoresce under the Wood light for weeks or months after the rest of the affected area has cleared Hairs may cease to fluoresce temporarily, only to show up at a later examination Among the factors believed to play a part in this stubborn chronicity of the disease have been mentioned the presence of infected loose scales, the removal of healthy hairs, so that the follicles are left open for invasion by the organisms, and, finally, the breaking off of diseased hair with a portion of the infected hair left in the follicle to infect the new hair as it forces its way to the surface

The present study is not intended as a brief for manual epilation as a curative treatment for tinea capitis As a matter of fact, it has been truly stated that any treatment of this disease is still in the experimental stage

Spontaneous cure of tinea capitis occurs at the age of puberty and in younger children in from 10 [3f] to 27 [5] per cent of cases For this reason the real contribution of any therapeutic measure will be exceedingly difficult to assess

One of the chief stumbling blocks in the application of manual epilation as a treatment for tinea capitis in the past was the degree of training and experience required to distinguish infected hairs from normal hairs, thus enabling one to select the proper areas for epilation. Some claimed that the diseased hairs could be recognized by a reddening about the follicular orifice, others applied chloroform to the scalp, claiming that with it infected hairs assumed a whitish appearance This difficulty was overcome, in 1903, when the Wood filter lamp was introduced Under ultraviolet light the diseased hairs become fluorescent and can be easily distinguished from normal hairs Manual

4 Rothman, S , Smiljanic, A , Shapiro, A L, and Weitkamp, A W · Spontaneous Cure of Tinea Capitis in Puberty, J Invest Dermat 8 81-98 (Feb) 1947

5 Livingood, C S, and Pillsbury, D M Ringworm of the Scalp, J Invest. Dermat 4 43 (Feb) 1941

DISSEMINATE LUPUS ERYTHEMATOSUS

HAMILTON MONTGOMERY, M D
AND
WILLIAM G McCREIGHT, M D
Fellow in Dermatology and Syphilology, Mayo Foundation
ROCHESTER, MINN

DISSEMINATE lupus erythematosus is to be regarded as a systemic disease which in its acute form usually terminates fatally Cutaneous manifestations do not always predominate, they may be transitory and even in a few cases absent throughout the course of the disease, in which instances one speaks of "lupus erythematosus without cutaneous lesions"

The purpose of this paper is to review the cases of disseminate lupus erythematosus seen at the Mayo Clinic up to 1948 An analysis of 154 cases of disseminate lupus erythematosus up to 1938, together with a review of the literature, was given in "Oxford Medicine [1]" This survey included a compilation of various studies and papers over a period of years by Goeckerman, Keith and Rowntree, O'Leary, Brunsting and one of us (H M) A subsequent report was made in a symposium on lupus erythematosus by Kierland, Montgomery, Stickney, Keith, Slocumb and O'Leary [2] An analysis of 132 cases of disseminate lupus erythematosus seen at the clinic from 1938 through 1947 is presented here This includes studies of the so-called lupus erythematosus cell seen in the bone marrow, as described by Hargraves and his associates [3]

Analysis of various findings in disseminate lupus erythematosus has obviously called for the cooperation of many of our associates in various departments of the clinic It is impossible to touch on all phases

Dr Montgomery is in the Section on Dermatology and Syphilology, Mayo Clinic

Read at the Sixty-Eighth Annual Meeting of the American Dermatological Association, Inc, San Diego, Calif, April 27, 1948

1 Montgomery, H Disseminate Lupus Erythematosus as a Systemic Disease, in Christian, H A Oxford Medicine, New York, Oxford University Press, 1939, vol 4, pt 1, chap 1-C, pp 44 (41)-44 (65)

2 Kierland, R R , Montgomery, H , Stickney, J M , Keith, N M , Slocumb, C H, and O'Leary, P A Symposium on Lupus Erythematosus, Proc Staff Meet, Mayo Clin **15** 675-688 (Oct 23) 1940

3 Hargraves, M M , Richmond, H , and Morton, R Presentation of Two Bone Marrow Elements The "Tart" Cell and the "L E" Cell, Proc Staff Meet, Mayo Clin **23** 25-28 (Jan 21) 1948

Special attention was given to the epilation of the mother patch or patches, the name given to the area or areas of greatest involvement in the infection When epilation was concentrated in this area, many of the scattered infected hairs in other areas were spontaneously cured In addition, it was noted that if manual epilation was not stressed in these areas progress was slow

Hairs were removed with plain cilia forceps

A follow-up examination with the Wood filter after four months was used as a criterion of cure

RESULTS

Of the 39 patients in the first, or control, group treated exclusively with ointment, 11, or 22 8 per cent, were cured Of the 17 patients in the second group, given one minute epilation every two weeks in addition to the ointment treatment, 6, or 35 2 per cent, were cured Of the 32 patients in the third group, given manual epilation for five minutes every two weeks, in addition to the ointment treatment, 18, or 56 2 per cent, were cured

In the control group, the time required for cure in 9 cases varied from 98 to 293 days, the average being 193 4 days In group 2, the time required for cure in 6 cases varied from 72 to 243 days, the average being 171 5 days In group 3, the time necessary for cure in 18 cases varied from 46 to 384 days, with an average of 185 5 days

In view of the variation in the individual patient's response to treatment, together with the wide variations in extent of involvement of infections with this disease, it is difficult to correlate the time necessary for cure in each group with the total time spent in manual epilation in that group However, group 3 included a large number of patients with extensive involvement of the scalp, and previous to this study many of them had been subjected to various types of treatment

Regardless of the length of time treated, the patients for whom manual epilation was used improved continuously under treatment Only patients with very extensive infection failed to respond, and even in such patients, if the treatment is continued for a sufficient period, the infection can be eradicated

SUMMARY

Three groups of patients with tinea capitis were treated

In the control group, who had no manual epilation, 22 8 per cent of the patients were cured Of the patients who were given epilation for about one minute every two weeks, 35 2 per cent were cured Of the patients who were given epilation for five minutes every two weeks, 56 2 per cent were cured

It is concluded that manual epilation is definitely of value in the treatment of tinea capitis, regardless of other methods used

2013 Delancey Street

of the various papers just mentioned and are also made in the seventh edition of Ormsby and Montgomery's text[7] and will not be taken up further in this paper

TABLE 2.—*Analysis of One Hundred and Thirty-Two Cases of Disseminate Lupus Erythematosus (1938 Through 1947)*

Data	Type of Disseminate Lupus Erythematosus		
	Chronic (23 Cases)	Subacute (77 Cases)	Acute (32 Cases)
Women, per cent	83	87	91
Onset as discoid type, per cent	30	17	6
Average age at onset, years	33	35	27
Average age at onset of dissemination, years	34	36	28
Prodromal symptoms, per cent	5	14	41*
Sensitivity to light, per cent	56	40	22
Arthralgia or arthritis, per cent	43	71	91
Anemia (less than 4,000,000 erythrocytes per cubic millimeter or less than 12 Gm hemoglobin), per cent	35	54	91
Leukopenia (less than 5,000 leukocytes per cubic millimeter), per cent	30	67	81
False positive flocculation or Wassermann reaction, per cent	17	25	44
Renal irritation, nephrosis or nephritis, per cent	39	69	100
Albumin	39	56	100
Erythrocytes	9	34	81
Casts	4	17	69
Deaths attributable to the disease, per cent	4	35	84†

* Five patients had no cutaneous lesions when first seen here (lupus erythematosus without cutaneous lesions)

† Five patients were still alive at last report One had completely recovered, having been followed for five years with no evidence of the disease for eighteen months One was a semi invalid followed for thirteen and one half years after the onset of disease seven and one half years after dissemination Efforts to follow up 3 patients were unsuccessful, and the chances are that these persons are dead

TABLE 3.—*Analysis of Other Laboratory Data in One Hundred and Thirty-Two Cases of Disseminate Lupus Erythematosus (1938 Through 1947)*

Data	Type of Disseminate Lupus Erythematosus					
	Chronic		Subacute		Acute	
	Number	Per Cent	Number	Per Cent	Number	Per Cent
Sedimentation rate, mm per hour	20		70		31	
Normal, 0-20		35		14		0
Mildly increased, 21 40		25		16		3
Moderate, 41 60		25		21		19
Rapid, 61 or more		15		49		78
Serum proteins (total)	2		33		22	
Normal, 6-8 Gm per 100 cc serum		50		79		64
Total proteins, less than 6 Gm per 100 cc serum		50		6		32
Total proteins, more than 8 Gm per 100 cc serum		0		15		4
Albumin globulin ratio	2		31		18	
Normal, 1 5 1–3 1		50		16		6
Ratio less than 1 5 1		50		84		94

We have kept the classification employed by O'Leary, which is similar to that previously used by Madden, of dividing cases of disseminate lupus erythematosus into chronic, subacute and acute types

7 Ormsby, O S, and Montgomery, H Diseases of the Skin, ed 7 Philadelphia Lea & Febiger 1948

administered the treatment Moreover, of seventeen fungicides tried by the Public Health Service, the most efficacious was selected, the one used by Dr Wilson ranked seventh among these These differences are sufficient to account for the increased percentage of cures and the shorter time required for a cure reported by the Public Health Service The fungicide which proved most efficacious was a mixture of 5 per cent salicylanilid® (a compound formed by heating a mixture of salycylic acid, aniline and phosphorus trichloride), a powerful industrial fungicide, and 1 per cent hyamine (a quaternary ammonium compound) 1622, a fungicide and cationic detergent, in carbowax 1500® (a mixture of polyethylene glycols), a water-soluble waxy substance with penetrant properties

Almost as efficient was a mixture of 5 per cent copper undecylenate in carbowax 1500,® or 5 per cent copper undecylenate in carbon tetrachloride, a powerful solvent, with fungicidal properties, which helps to carry the fungicide into the follicles

The treatment consisted in placing the child under a Wood light every school day and pulling out with forceps the fluorescent hairs in small isolated patches and in epilating conspicuously loose fluorescent hairs in the larger infected areas, before rubbing in the fungicide The hair was clipped with electric clippers every ten days

Dr T Benedek, Chicago I think it was worth while to recall the usefulness of a technic which up to fifty years ago, though painful and tedious, had been the only method of treatment of tinea capitis of the scalp This technic is not the method of choice, yet it has retained its usefulness in certain instances, as in removal of a few scattered infected hairs on the scalp or, in the case of roentgen epilation, of a few hairs at the curved edges of the hair line not reached by the radiation There is even an absolute indication for manual epilation when the eyebrows and/or eyelashes are infected concurrently with a microsporum infection of the scalp I had 3 cases of this kind, in 2 the eyebrows were infected and in the third numerous eyelash hairs of the upper lid of one eye were infected These hairs were epilated manually under Wood light, and the regrown hairs were normal

I should like to ask Dr Wilson whether he carried out cultural investigations in connection with the application of undecylenic ointment If so, I would like to know the result of such studies during the four month follow-up period It would be interesting to know the shortest period within which the hairs treated with undecylenic ointment did not show any cultural response and the longest period within which the hairs so treated still yielded a culture of the organisms

I carried out similar investigations with salicylanilid® ointment, introduced by Schwartz and his associates In 40 consecutive cases of M audouini infection of the scalp, hairs were epilated under Wood light every two weeks, for cultural control Fifteen to eighteen hairs from different foci were distributed in three glucose agar slants Each hair yielded a normal colony of M audouini, without the slightest retardation of growth, as compared with untreated hairs infected with M audouini used as controls For periods up to 112 days these hairs infected with M audouini which were treated with salicylanilid® yielded normal colonies, without even the slightest retardation of growth, which at least was anticipated Salicylanilid® caused severe irritation in the form of suppurative folliculitis when applied after roentgen irradiation This reaction, however, was seen, peculiarly, only in areas of infected hairs

In this group of cases were three families, in two of which one sibling, and in the third two siblings, were infected during the treatment with salicylanilid® of the first affected sibling All these observations reveal, obviously, that there is at present still one method of choice for the treatment of tinea capitis, that is, the Kienbock-Adamson five point method of total epilation

lymph nodes and other organs and in which all combinations in extent and severity of the process may occur

The diagnosis of lupus erythematosus without cutaneous manifestations is difficult to make All the patients whose cases are included in table 2 presented evidence of cutaneous lesions at some time during the course of the disease There are approximately 6 additional cases that were encountered in the period from 1938 through 1947 in which the diagnosis of lupus without cutaneous lesion was entertained because of various systemic manifestations and laboratory findings In 2 of these cases, further observations suggested the diagnosis of periarteritis nodosa and dermatomyositis, respectively, and in 4 cases a diagnosis of disseminate lupus erythematosus seemed justifiable, there being lupus erythematosus cells in sternal marrow obtained by aspiration in 3 cases

There can be no question that bona fide cases of lupus without cutaneous lesions have been reported in the literature with or without their having had the features of the Libman-Sacks syndrome A patient who might be classified in this group and who is not included in this series was at the clinic in February 1948

She was a woman, aged 33, who had had recurrent arthralgias for eight years, had complained of abdominal pain and menorrhagia in January 1947 and had exhibited edema of the feet and ankles and decreased urinary output in May 1947 In August 1947 she had had furuncle-like lesions that were generalized but worse on the extremities than on other parts of the body and which cleared with antibiotic treatment Later, there had been a recurrence of a few of the lesions on the feet When seen at the clinic, the patient apparently had no cutaneous lesions of any sort It is possible that the lesions that she had could have been purpuric, ulcerative or bullous lesions of lupus erythematosus, but this would seem unlikely The patient had been hospitalized from May 1947 because of severe anemia Reactions to transfusions had developed, and she had had a progressive downhill course with much edema, ascites and septic temperature The patient died early in 1948, five days after admission to the hospital with a sudden onset of severe headache and dyspnea Laboratory findings before death included albumin and erythrocytes in the urine and a blood urea of 118 mg per hundred cubic centimeters The concentration of hemoglobin was 5 4 Gm per hundred cubic centimeters of blood, erythrocytes numbered 3,160,000 and leukocytes 9,800 per cubic millimeter of blood The sedimentation rate (Westergren method) was 141 mm per hour, the Kline reaction was 1 plus and the Kahn, 3 plus, the total proteins measured 3 9 Gm per hundred cubic centimeters of serum, and the albumin-globulin ratio was 1 6 2 3 The clinical diagnosis was chronic glomerulonephritis with edema, ascites and hypertension (the blood pressure was 180 mm of mercury systolic, and 105 mm diastolic) Postmortem examination failed to reveal evidence of glomerulonephritis but showed pronounced wire loop changes in the kidneys, such as are frequently associated with lupus erythematosus, and also a nonbacterial verrucous endocarditis and a perisplenitis This case is reported, therefore, simply to illustrate the difficulties of diagnosis but, in retrospect, should probably be classified as one of lupus without cutaneous lesions

became loose after the third injection If proper attention was given by the parent, rarely more than six injections were necessary No ill effects were seen in the patients treated

DR LOREN W SHAFFER, Detroit I, too, believe in the value of epilation in the management of tinea capitis However, another factor, spontaneous cure, has not had sufficient emphasis, it should be taken into consideration in evaluating the effectiveness of any prolonged method of treatment A control group without treatment should be observed

We physicians in Detroit have had a rather unusual opportunity for studying the rate of spontaneous cure In 1945 Dr Lee Carrick made a spot survey on the incidence of tinea capitis in school children of Detroit On the basis of this survey, it was estimated that there were about 7,000 cases The management of these cases would have swamped our facilities No organized program for treatment was developed

This spring an attempt was made to find and examine the persons who had infections three years ago, in order to learn what has happened to them We found that a diagnosis of tinea capitis had been made in 1945 in 129 cases and that in all instances the infecting organism was M audouini We were much surprised to find that in 70 per cent of these cases the disease had gone on to what we assume to have been largely a spontaneous cure A few patients may have had fairly adequate treatment, but the great majority had had inadequate or no treatment Surprisingly, the rate of spontaneous cure was as high among the younger age group as among those near or at puberty

It is our impression now that the epidemic that was present in our city schools has been subsiding spontaneously, with very inadequate management from a medical and public health standpoint A survey is to be made again this fall to evaluate this impression

DR J WALTER WILSON, Los Angeles I want to repeat the warning I voiced at last year's Session regarding dangerous types of ultraviolet radiation for fluorescence examinations Cold quartz ultraviolet light burners produce 90 per cent of their energy at the level of 2,537 angstrom units This wavelength produces fluorescence beautifully in hairs infected with tinea capitis due to a microsporum, but it must not be forgotten that it is also capable of producing damage to the patient's eyes and scalp, as well as the backs of the operator's hands

It is possible to obtain a filter which changes 2,537 angstrom units to 3,650 angstrom units by means of a secondary phosphor, but the production of such a filter is apparently more expensive than many manufacturing concerns care to undertake Such a filter, however, would eliminate this danger, and one should insist on its being made available if a cold quartz source is to be used

DR JOHN F WILSON, Philadelphia Spontaneous cure was considered in the study, but the presence of a control group and the method in which the study was carried out should answer Dr Loren Shaffer's question

I would like to remind the Section that this paper is not presented in the form of a therapeutic approach to tinea capitis, but is offered simply as an attempt to standardize a long-accepted and valuable treatment of tinea capitis

for from five to eight or more years, these cases including some noted by the Mount Sinai group [8] In the group with subacute disseminate lupus erythematosus, as indicated in table 1, there was one subsequent death We were able to follow up a majority of this group through letters of inquiry or further observation of the patient

Table 3, which gives an analysis of some of the other laboratory data in the recent series of patients with disseminate lupus erythematosus, is self explanatory In some instances, so few examinations were performed that the percentage figures are of little significance In general, the sedimentation rate increased and the albumin-globulin ratio became reversed as the condition became more acute and severe (There were no determinations made of euglobulins) Thus, in the cases in which there were the highest sedimentation rates and reversal of the albumin-globulin ratio there was likely to be the greatest degree of false positive serologic reaction, without, however, our being able to attach any diagnostic significance to this phenomenon

Other laboratory procedures were performed in too small a series of cases to permit presentation in tabular form Positive blood cultures were obtained in 2 of 31 instances A green-producing streptococcus was obtained on blood culture in 1 case of acute disseminate lupus erythematosus, and a staphylococcus was obtained in 1 case of subacute disseminate lupus erythematosus

In 13 cases, determination was made of the total 17-ketosteroids present in a twenty-four hour specimen of urine In 1 case of acute and in 1 case of the chronic disseminate type of lupus erythematosus, ketosteroids measured less than 4 mg per hundred cubic centimeters for twenty-four hour specimens In a series of 11 cases of the subacute type of lupus erythematosus, 5 women and 1 man had values of less than 4 mg for twenty-four hours, whereas 5 women had values of more than 4 mg in twenty-four hours The amount of 17-ketosteroids, therefore, seemed to be without diagnostic significance and probably was indicative only of the toxic manifestation of a debilitating disease

Aspiration of sternal marrow was attempted in 26 cases Of 7 cases classified as of acute disseminate lupus erythematosus, aspirated sternal marrow was reported as positive for lupus erythematosus cells in 5 cases In 1 case observations were suggestive of lupus erythematosus cells, and in 1 case the attempt at aspiration was unsuccessful The 5 patients in this group who had lupus erythematosus cells and the 1 in whose marrow there were cells resembling lupus erythematosus cells are known to have died There were 18 patients with subacute disseminate lupus erythematosus who had aspirations of sternal marrow

8 Baehr and Pollack [4] Klemperer [7]

because there are various aspects of the subject that call for more intensive study by various internists, as well as by pathologists and other laboratory workers Thus, for example, the number of cases that should be classified with the Libman-Sacks syndrome with special reference to nonbacterial rather than bacterial verrucous endocarditis, or the number of cases that should be classified as true nephritis rather than simple renal irritation, or a detailed analysis of post-mortem findings, necropsy having been performed in 32 of the cases, will not be given in detail

The concept of lupus erythematosus as a collagenous disease, which view has been championed by the Mount Sinai group, is summarized in recent papers by Baehr and Pollack,[4] by Klemperer [5] and

TABLE 1.—*Analysis of One Hundred and Fifty-Four Cases of Disseminate Lupus Erythematosus (up to 1938)*

Data	Type of Disseminate Lupus Erythematosus		
	Chronic (80 Cases)	Subacute (44 Cases)	Acute (30 Cases)
Women, per cent	61	80	77
Onset as discoid type, per cent	60	34	33
Average age at onset, years	32	30	21
Average age at onset of dissemination, years	39	38	28
Lesions of mucous membranes, per cent	18	23	43
Prodromal symptoms, per cent	5	27	33
Sensitivity to light, per cent	22	23	23
Arthralgia or arthritis, per cent	20	57	63
Fever, per cent	5	57	97
Anemia (less than 4,000,000 erythrocytes per cubic millimeter of blood or a concentration of hemoglobin of 70 per cent or less), per cent	20	52	84
Leukopenia (less than 4,500 leukocytes per cubic millimeter), per cent	22	43	71
False positive flocculation or Wassermann reaction, per cent	6	11	17
Renal irritation, nephrosis or nephritis, per cent	3	18	32
Infected tonsils, per cent	68	54	40
Deaths attributable to the disease, per cent	8	47	100

in as yet unpublished studies by Baehr and Jarcho ("Oxford Medicine") The literature regarding disseminate lupus erythematosus has become voluminous In a five year period, Hench and his associates [6] found fifty-two references to disseminate lupus erythematosus which pertained to associated arthralgias or etiologic concepts regarding the disease, or both References to significant articles are given in the bibliographies

4 Baehr, G, and Pollack, A D Disseminated Lupus Erythematosus and Diffuse Scleroderma, J A M A **134** 1169-1173 (Aug 2) 1947

5 Klemperer, P The Pathogenesis of Lupus Erythematosus and Allied Conditions, Ann Int Med **28** 1-11 (Jan) 1948

6 Hench, P S , Bauer, W , Boland, E W , Crain, D C , Freyberg, R H , Graham, W , Holbrook, W P , Lockie, L M , McEwen, C , Rosenberg, E F , and Stecher, R M Rheumatism and Arthritis II Review of American and English Literature of Recent Years (Ninth Rheumatism Review), Ann Int Med **28** 309-451 (Feb) 1948

PATHOLOGIC FACTORS

The pathogenesis of lupus erythematosus and allied conditions has been discussed in recent articles by the Mount Sinai group in New York, and detailed reasons have been given for regarding these conditions as collagenous diseases associated primarily with fibrinoid degeneration of collagen Baehr and Pollack, and Klemperer, though they called attention to fibrinoid degeneration in lupus erythematosus and scleroderma, recognized that these conditions are distinct from one another and also that they are not related to rheumatic fever, rheumatoid arthritis, serum sickness, periarteritis nodosa or thromboangiitis obliterans, in which similar collagenous changes may be seen on pathologic examination In cases in which postmortem examinations were performed in the original series of 154 cases and on which Stickney's observations were based, wire loop changes in the kidneys, including hyaline and fibrinoid degeneration in the basement membrane of the glomerular capillaries, were relatively absent There was no clearcut case of nonverrucous bacterial endocarditis, although subsequent study of 1 of 6 cases changed the diagnosis from bacterial to nonbacterial endocarditis Postmortem findings in some cases of the second series, as well as in cases in the first series, were reviewed by Correa [12] It would appear not only from our own records but also from other reports in the literature that in an increasing number of cases, possibly half of the reported cases with autopsy, there is observed fibrinoid degeneration of the collagen, including the vascular changes previously emphasized by Klemperer and his associates in regard to changes occurring in the kidneys and heart Similar changes are much less frequent in the spleen and other organs Whether these changes are primary or of toxic nature remains open to debate

One of us (H M) has written several articles on the cutaneous changes in disseminate lupus erythematosus and has found little evidence of collagenous change, including fibrinoid degeneration and obliterative changes in superficial vessels in the skin We have reviewed cutaneous specimens for biopsy of 96 lesions of disseminate lupus erythematosus, 25 lesions from 22 cases of chronic types, 53 lesions from 41 cases of subacute types and 18 lesions from 16 cases of acute types Details of these studies will be the subject of a subsequent report [13] This series included specimens for biopsy on

12 Correa, D H Pathology of Disseminated Lupus Erythematosus with Special Reference to the Vascular Changes, Thesis, Graduate School of the University of Minnesota

13 These will appear in a thesis to be submitted by Dr McCreight to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Dermatology

The chronic type has also been termed the "generalized discoid" type, or, in other words, discoid lupus erythematosus in which lesions occur elsewhere than on the face Chronic discoid and generalized disseminate lupus erythematosus are usually regarded as cutaneous diseases, with few, if any, constitutional symptoms One can see, however, from tables 1, 2 and 3 that constitutional symptoms are present in a number of cases of chronic disseminate lupus erythematosus The classification of what most writers term "disseminate lupus erythematosus" into subacute and acute phases is a rather arbitrary one, based on the degree of severity of the systemic findings and on a period of observation The classification in the original group resulted from unpublished studies by O'Leary and Rogin and discussion by one of us (H M) with O'Leary as to where to group certain cases A similar plan was carried out in the analysis of the recent series of 132 cases, an attempt being made to maintain the same criteria in regard to classification

ANALYSIS OF CLINICAL AND LABORATORY FINDINGS

We believe a brief discussion of the similarities and discrepancies between tables 1 and 2 to be of value Some of the discrepancies are obviously mathematical, as there are too few cases in the various groups for the data to be presented accurately on a percentage basis Some of the discrepancies undoubtedly arise from the changing concept of the disease, a difference in attitude including the fact that internists as well as the members of the section on dermatology at the clinic have become more lupus erythematosus-conscious, as a result of which there are many more cases reported in the later series, especially of the acute disseminate form, in which cutaneous manifestations were minimal or transitory Increasing predominance of the disease in women in the recent series fits in with reports of series elsewhere in which an incidence as high as 95 per cent has been reported in women (Baehr, "Oxford Medicine") The finding of only 6 per cent of the acute cases in which the disease started as the chronic discoid type instead of the observation of 33 per cent in which it did so in the older series is probably explainable on the basis of the present recognition of acute fulminating forms of the disease with minimal cutaneous manifestations, which forms previously would have been considered chronic This observation does not imply, however, that chronic discoid and acute disseminate lupus erythematosus are two different diseases, as some writers would maintain, because all transitions may be seen both clinically and pathologically in cutaneous lesions This situation is comparable to that observed in sarcoidosis in which there may be lesions limited to the skin or limited to the bones, lungs,

ETIOLOGIC FACTORS

We do not wish to repeat all the multiple etiologic factors to which disseminate lupus erythematosus has been attributed In both the old and the recent series, tuberculosis played an insignificant role, although one may encounter an occasional case in which a tuberculous infection may be superimposed on disseminate lupus erythematosus and result in death We agree with Baehr and his associates that the concept of lupus erythematosus being of tuberculous origin should be abandoned, although this concept apparently still persists in some of the European writings

There have been several recent articles in the literature dealing with the effect of pregnancy and endocrine disturbances on lupus erythematosus We have seen acute lupus erythematosus develop after normal pregnancy and run a rapidly fatal course, and we have had patients who showed temporary improvement after oophorectomy After review of cases of various types of disseminate lupus erythematosus associated with pregnancy, we believe that pregnancy may, at the most, be merely a contributing factor and we agree with O'Leary, who stated in a discussion of Baehr and Pollack's paper that "therapeutic castration of women who have disseminate lupus erythematosus has been valueless in my experience" Baehr,[4] in a discussion of his paper with Pollack, also stated that treatment of disseminate lupus erythematosus with testosterone propionate or castration in women has not materially altered the course of the disease and that he had not seen any evidence of endocrine disorder in men having disseminate lupus erythematosus Baehr and Pollack stated the belief that the predominance of the disease in women merely represents a sex predisposition similar to the predisposition for men seen in thromboangiitis obliterans They also express opposition to the acceptance of an allergic basis for lupus erythematosus There were no patients in either of our series in whom an allergic factor predominated unless we include those patients who were sensitive to light

We have already stated our views against regarding lupus erythematosus as primarily a collagenous disease We believe that there may be multiple etiologic factors and that toxic changes of unknown nature may predominate In other words, the etiology of lupus erythematosus remains to be determined

DIAGNOSIS

The diagnosis of localized discoid and chronic disseminate lupus erythematosus is usually readily made on the basis of the clinical appearance of the lesions In many cases of subacute or acute disseminate lupus erythematosus, small areas with characteristic scaling and plugging may be recognized The combination of erythematous involvement of the face and finger tips is also almost pathognomonic

To continue with the comparison of tables 1 and 2, the 22 per cent incidence of sensitivity to light found in the acute disseminate cases corresponds with recent reports in the literature that a light-sensitive factor does not necessarily predominate and need not even be considered a factor in acute disseminate cases There still remain, however, many cases in which dissemination of chronic discoid or subacute disseminate lupus erythematosus has resulted from exposure to light

We purposely omitted from table 2 any figures regarding lesions of the mucous membranes, incidence of fever and the percentage of patients with infected tonsils because the association of these conditions is generally accepted Some of the changes regarding the percentage of patients with leukopenia result from our acceptance in the later series of 5,000 leukocytes per cubic millimeter, rather than 4,500 leukocytes per cubic millimeter, as the lower limit of normal (a value which apparently is now accepted in hemocytologic texts) The increase of false-positive serologic reactions seen in table 2 may be explained on the basis of the fact that in practically all the cases in the recent series not merely a single serologic test for syphilis, but a battery of four tests, including the Kahn, Kline, Hinton and Kolmer tests, was given This was not usually true of the first series As was remarked, however, in the chapter by one of us (H M) in "Oxford Medicine," results of serologic tests for syphilis seemed to become increasingly positive in a given person, the increase depending on the acuteness of the disease In several cases in the acute disseminate group in the recent series the reaction of all four tests was strongly positive Disseminate lupus erythematosus should definitely be grouped with the diseases causing false positive serologic reactions

In table 1 evidence of renal irritation, nephrosis or nephritis was based on a rather critical analysis of the various urinary findings, however, it was felt advisable simply to tabulate the urinary data in the present series Observations regarding elevated blood urea and hypertension with or without renal disease remained in the recent series essentially as given in the chapter in "Oxford Medicine" and summarized in papers by Keith and Stickney,[2] as part of a symposium, but are subject to further analyses

In regard to deaths attributable to the disease, in table 1, as was originally reported in "Oxford Medicine," 2 patients of those with the acute form were alive Both of these patients died subsequently, although 1 remained alive for eight years after the onset of the acute disseminate lupus erythematosus The footnote on table 2 regarding deaths in the recent series is self explanatory Though duration of life in the group with the acute form of the disease may be a matter of only a month and death usually occurs within a year, there are increasing but isolated cases reported in which the disease has persisted

there is likely to be more edema about the eyelids, with a heliotrope-like coloring, than in lupus erythematosus Weakness and atrophy of the muscles are not prominent features of lupus erythematosus but are characteristic of dermatomyositis From the laboratory aspects, dermatomyositis is not associated, as a rule, with leukopenia, anemia or false positive serologic reactions, on the other hand, it is associated with creatinuria

Distinction of early or mild forms of disseminate lupus erythematosus from cases of sunlight dermatitis (eczema) must be made on the basis of concomitant findings In patients who have a sensitivity to sunlight various degrees of dermatitis, as well as decided malaise and constitutional symptoms, may develop after exposure to the sun, but this group of patients should be sharply distinguished from patients with lupus erythematosus who also may be sensitive to the sun

TREATMENT

There is no satisfactory treatment of disseminate lupus erythematosus Avoidance of exposure to the sun, prolonged rest in bed and various supportive measures directed to the constitutional symptoms are indicated We have not found the use of sulfonamide compounds or penicillin to be of value

SUMMARY AND CONCLUSIONS

Disseminate lupus erythematosus, especially the acute and subacute types, must be regarded as a systemic disease Cutaneous manifestations may be minimal or even absent Analysis is given of 154 cases of disseminate lupus erythematosus encountered up to 1938 and of 132 cases of disseminate lupus erythematosus encountered from 1938 through 1947 The following observations are worthy of emphasis False positive reactions in Wassermann or flocculation tests occur in increasing percentage according to the acuteness of the disease, as also do increase of the sedimentation rate and reversal of the albumin-globulin ratio It would appear that the presence of the so-called lupus erythematosus cells in sternal aspirations of bone marrow is of diagnostic and prognostic value in cases of acute disseminate lupus erythematosus with or without cutaneous lesions However, a large series of cases should be studied and further observations should be made in this regard Studies of the histologic changes in the skin in various types of disseminate lupus erythematosus show only minor changes in the collagen or fibrinoid degeneration in the walls of the vessels We should prefer, therefore, not to regard lupus erythematosus primarily as a collagenous disease but to continue to regard the cause as unknown We found little evidence to support the

For 12 of these the aspirated marrow was negative for lupus erythematosus, for 3 it was positive, and for 1 it was suggestive One patient had two aspirations, lupus erythematosus cells not being demonstrated in the first specimen and leukemic reticuloendothelial cells being reported in the second Aspiration of sternal marrow was unsuccessful in 1 patient on six different attempts Sternal aspiration was negative for lupus erythematosus cells in 1 case of chronic disseminate lupus erythematosus Lupus erythematosus cells, as described by Hargraves and his associates, appear to predominate in cases of disseminate lupus erythematosus in which the disease is active or increasing and are not demonstrable, as a rule, if the condition is quiescent So far, lupus erythematosus cells have not been reported as occurring in any other condition except in 1 case of multiple myeloma [9] Further observation of a large series, however, will be necessary for their status and diagnostic significance to be determined

Analysis or comparison of various systemic manifestations found in the two series of cases does not show any fundamental variations of the recent series from those reported for the first series in "Oxford Medicine" or from those cited in recent articles in the literature, which are quoted in recent reviews [10] Reports of ocular findings, as seen at the clinic and elsewhere, were recently reviewed by Wagener [11] Gastrointestinal symptoms have been minimal in the present series of 132 cases We should like, however, to emphasize that there have been several cases with symptoms which involved the central nervous system and which were not terminal manifestations but were encountered early in the course of acute or subacute disseminate lupus erythematosus The symptoms in 1 case included headaches, choked disks and palsy of the face, with evidence at postmortem examination of endarteritis of the cerebral vessels In another case, there were cerebrothrombosis, convulsions, aphasia and weakness in a girl aged 16 years, who also had evidence of anemia, an increased sedimentation rate renal irritation and false positive serologic reactions Another patient had nervous irritability and development of a cerebral accident with convulsions and euphoria, when seen a year later, she had typical lesions of lupus erythematosus of the scalp and body, and aspirated bone marrow was positive for lupus erythematosus cells Although the tendency has been to focus attention on the cardiac, renal, hepatic, splenic or arthritic involvement in lupus erythematosus, it is evident that any organ in the body may be involved in the process

9 Hargraves, M M Personal communication to the authors

10 Baehr and Pollack [4] Klemperer [5] Hench and others [6] Ormsby and Montgomery [7]

11 Wagener, H P Retinal Lesions in Acute Disseminate Lupus Erythematosus Am J M Sc **211** 240-244 (Feb) 1946

be disregarded Finally, there is the possible role of heavy metals, as has been commented on by a member of this association

The solving of the problem of any one of the diffuse collagen diseases may well be the key to all

DR JOHN F MADDEN, St Paul I had the opportunity to read Dr Montgomery's paper It represents a tremendous amount of work on the largest number of cases of this disease studied by one author I should like to emphasize the following points The Hargrave, or lupus erythematosus, cell is most numerous and most often found in acute cases This fact is a great diagnostic aid, especially in cases of lupus erythematosus without cutaneous manifestations The high incidence of false positive serologic reactions in cases of acute lupus erythematosus should be constantly kept in mind Many autopsies have been made in cases of acute lupus erythematosus, but I was unable to find a record of a single autopsy in all the hospitals in St Paul and Minneapolis made in cases of chronic lupus erythematosus in which there was death from any cause The disease wasn't even mentioned on autopsy records A careful study should be made of the autopsy findings in cases of chronic lupus erythematosus In some cases of acute lupus erythematosus there is extensive muscle damage, which can be observed at biopsy My associates and I will report on this subject in detail later I enjoyed Dr Montgomery's paper very much

DR. H J TEMPLETON, Oakland, Calif Acute disseminated lupus erythematosus is an edema-producing disease The edema of the face paints a rather typical clinical picture Edema of the brain accounts for many of the nervous symptoms, even convulsions and coma Edema of the lungs occurs in terminal cases Edema of the abdominal organs probably accounts for the abdominal pain which occasionally is found in this disease

A physician's son, with the fulminating type of the disease, had such intense abdominal pain that a surgical consultant wished to do an exploratory laparotomy It was with considerable difficulty that I convinced the physician-father and the surgeon that the pain was caused by the lupus erythematosus and that surgical intervention was contraindicated I had previously seen the same diagnostic problem in a young woman, in whose case autopsy was performed The extremely acute edema of nearly all the abdominal viscera explained her severe abdominal pain

I know of no absolute criterion for differentiating the pain of acute disseminated lupus erythematosus and that caused by a "surgical abdomen" The most important point is the knowledge of the dermatologist that acute disseminated lupus erythematosus can produce such pain The surgeon generally does not have this knowledge

DR MAURICE J COSTELLO, New York I have recently had the opportunity to study a woman 31 years of age in whom acute lupus erythematosus of the disseminate type developed She had had a splenectomy in 1945 for thrombopenic purpura

For some time thereafter she complained of fatigue and pain and swelling of the finger joints Within a month or two an eruption appeared which was generalized, roughly symmetric and intensely pruritic, the lesions occurring in groups of papules and vesicles

When I first saw the patient, in August 1947, she stated that the eruption had been present uninterruptedly for about eighteen months The eruption was that of dermatitis herpetiformis Sulfapyridine was not prescribed because of her past history of purpura, the presence of splinter hemorrhages of the sides of the terminal

which previous reports were based Special stains for connective tissue were employed in many cases

Briefly, we were able to find alteration of collagen, including fibrinoid changes in the walls of the vessels in the skin and around the connective tissue in the cutis, in less than one fourth of the cases, respectively, of chronic, subacute and acute disseminate lupus erythematosus In only 1 or 2 cases in each of the groups were there collagenous changes comparable in extent to those usually seen in the so-called wire loop lesions in the kidneys In the rest of the cases in which fibrinoid degeneration could be demonstrated, it was minimal and no greater than is seen in many other chronic inflammatory infectious diseases of the skin We submitted all sections showing fibrinoid changes to Dr Bennett of the section on pathologic anatomy of the clinic, who examined them independently and also found very slight amounts of changes, including fibrinoid changes, in the blood vessels

There is no question that in disseminate lupus erythematosus the superficial capillaries are dilated and often the walls of both venules and arterioles are edematous and also that there is destruction of both connective and elastic tissue by the inflammatory reaction in the cutis Basophilic degeneration and merging of collagen and elastic fibers to form collacin, as one of us (H M) previously emphasized, are seen only in lesions from the exposed parts of the body and then are not predominant in the disseminate group, as these changes may occur in the discoid group We still believe that the histopathologic diagnosis of disseminate lupus erythematosus can be made in the majority of cases if a specimen for biopsy is taken from a lesion that has not been subject to treatment and that is at least of several weeks' duration All transitions between chronic discoid and acute disseminate lupus erythematosus, as they were illustrated in previous papers, were again encountered

The Mount Sinai group in New York have stated that fibrinoid degeneration of collagen is not a pathologic process of sufficient specificity to serve as a reliable common denominator for classification of diseases The minimal changes in the collagen in cutaneous manifestations of disseminate lupus erythematosus raise the question as to how important a role collagenous disease plays in lupus erythematosus The skin, of course, is one of the organs most richly endowed with collagenous material On the other hand, we are heartily in accord with the Mount Sinai group regarding emphasis on collagenous disease in scleroderma In scleroderma, there are obliterative changes in the vessels with fibrinoid degeneration of the collagen and diffuse proliferative and degenerative changes in the collagen throughout the cutis

lation band This band should be shifted to the left, from a normal value of 6 to 4 or 2 or even 0, in acute exudative disease of any sort, but it is shifted to the right, to 7 or 8, in almost all cases of disseminated lupus erythematosus Also, the pain in these cases is likely to be relieved very little by morphine and rather promptly by ephedrine, epinephrine or even antihistaminic drugs Dr Costello made a remark that interested me particularly My colleague, Dr Harold Johnson, has observed in a number of cases of this disease that splenectomy (originally performed in 2 cases as a life-saving measure, to combat an associated thrombopenic purpura) was followed by prompt remission of the disseminated lupus I have undertaken this operation in 2 cases, in neither one of which the patient had thrombopenia, and both patients have experienced a remission, though 1 subsequently had a relapse, she is still getting along fairly well and has had no recurrence of leukopenia

DR HAMILTON MONTGOMERY, Rochester, Minn I wish to thank the discussers and I am essentially in accord with their emphasis on various other aspects of the disease, which time did not permit discussion of Because of the predominance of acute disseminate lupus erythematosus in young women, it was thought a cure might be obtained by therapeutic castration, but so far this treatment has been valueless We have seen no benefit from the use of testosterone There is no satisfactory explanation at present for the predominance of the disease in women any more than there is for the predominance of Buerger's disease (thromboangiitis obliterans), in men Some years ago, we studied a group of our cases for evidence of poisoning by heavy metals, including lead, with negative results I was glad to have the point brought up about muscle changes in disseminate lupus erythematosus The majority of cases with muscular atrophy and weakness of the major muscles have proved to be cases of dermatomyositis We recently had 1, however, which histologically and clinically in the beginning was one of disseminate lupus erythematosus and in which clinical features of dermatomyositis subsequently developed, while the cutaneous changes remained those of lupus erythematosus and not the toxic changes in the skin seen in dermatomyositis Unfortunately, no specimen for biopsy of the muscle was taken In the older series of cases, there were several cases of disseminate lupus erythematosus in which abdominal pain was an outstanding complaint Dr Goeckerman referred to these cases in a paper written many years ago In regard to Dr Templeton's suggestions regarding edema in the brain, in 2 of the cases referred to in the paper with symptoms of brain tumor or other neurologic disturbances postmortem examination was done, definite inflammatory changes in the brain being observed in both cases In regard to Dr Costello's remarks regarding splenectomy, it is true that patients with disseminate lupus erythematosus may be allergic in a broad sense In acute cases one must be cautious regarding the removal of even one infected tooth It is important first to obtain a state of temporary remission or quiescence of the disease if possible before removing any foci of infection Various types of purpura have been reported in a few cases but were an uncommon manifestation in our group and were more likely to be terminal manifestations of the disease

It is in the more acute forms, in which there may be only a transitory erythema, that the diagnosis becomes more difficult, and this erythema may not necessarily involve the face Sometimes there is transient purpura, or there may be hemorrhagic lesions Diagnosis becomes more difficult when there are no cutaneous manifestations It must be borne in mind that lupus erythematosus, especially the acute disseminate type, may affect any organ in the body The diagnosis is to be seriously entertained even without cutaneous lesions when several of the following combinations or signs occur arthralgias or arthritis, cardiac symptoms, evidence of renal irritation or nephritis, associated with malaise, a septic type of temperature, leukopenia and secondary anemia, an increased sedimentation rate, *false-positive* reactions in Wassermann and flocculation tests, albumin, erythrocytes and, at times, casts in the urine, and reversal of the albumin-globulin ratio To this group we may add tentatively the demonstration of so-called lupus erythematosus cells on sternal aspiration One must also keep in mind that symptoms referable to the gastrointestinal tract or to the central nervous system occur in some cases as do ocular changes

It now appears that most cases of the Libman-Sacks syndrome, including nonbacterial verrucous endocarditis, wire loop lesions in the kidney and perisplenitis, or more than one of these manifestations, are essentially cases of disseminate lupus erythematosus Nonbacterial verrucous endocarditis, however, may occur in a good many other conditions entirely unrelated to lupus erythematosus [14] Conversely, many cases of disseminate lupus erythematosus do not reveal the features of the so-called Libman-Sacks syndrome

Disseminate lupus erythematosus may be confused with dermatomyositis, and there are cases reported in the literature in which the two conditions are supposed to be associated in the same person We had 1 case of subacute disseminate lupus erythematosus in which, four years after the onset of the disease, dermatomyositis apparently developed, with pronounced weakness and wasting of the major muscles of the trunk, although a specimen for biopsy from the skin still revealed the histologic picture of subacute disseminate lupus erythematosus Biopsy of a specimen of the muscle revealed dermatomyositis As a rule, lupus erythematosus and dermatomyositis can be distinguished The cutaneous lesions of dermatomyositis, although histologically simulating those associated with acute disseminate lupus erythematosus, show merely a toxic dermatitis and fail to reveal liquefaction degeneration of the basal cell layer, keratotic plugging and other features of lupus erythematosus *Clinically*, in dermatomyositis

14 Kernohan, J W Personal communication to the authors

werger and associates[6] reported 6 additional cases of dermatitis venenata in nurses who had had prolonged contact with streptomycin In all cases there was an initial erythema followed by pruritus and a papulovesicular eruption, and, in addition, in 5 cases there was edema of the lids, associated with pruritus and photophobia Recently, we have been informed of a nurse at the Veterans Administration Hospital, Livermore, Calif, who, after prolonged contact with streptomycin, acquired a true exfoliative dermatitis[7]

In the course of the past two years 137 patients have been treated with streptomycin at this hospital Various lesions of the skin and mucous membranes have been seen in these patients and in nurses who have handled the drug The frequency and severity of the dermatologic complications occurring in patients vary with the dosage

The commonest cutaneous lesion is a generalized maculopapular erythematous rash with itching Any part of the body may be involved In severe cases the skin is very rough to the touch, feeling somewhat like sandpaper Pruritus is usually mild but may be extreme, so that the patient cannot rest until it is controlled Often, but not always, there is an associated eosinophilia The pruritus responds promptly to treatment with antihistaminic drugs, the rash usually does not This type of eruption is usually self limited, it occurs typically at the end of the first week of treatment, lasts for from five to ten days and then spontaneously clears In severe cases the eruption may last considerably longer There is no reason to discontinue treatment Six such cases occurred among 55 patients treated with 2 Gm daily, an incidence of 11 per cent, 1 among 16 patients treated with 1 Gm daily, an incidence of 6 per cent, and 2 among 66 persons treated with 0 5 Gm daily, an incidence of 3 per cent

Urticaria is rarer and may occur at any time after the first two weeks of treatment Both the urticaria and the associated itching can be controlled by the administration of antihistaminic drugs for a brief period However, the eruption often recurs as long as administration of the drug is continued In one instance extensive urticaria made its appearance after two weeks of treatment and continued until tripelennamine hydrochloride (pyribenzamine hydrochloride®) was given Treatment with tripelennamine hydrochloride was continued for the remainder of the course of streptomycin treatment and for one week more, with almost complete relief of symptoms When treatment with tripelennamine hydrochloride was stopped however urticarial wheals recurred,

6 Rauchwerger, S M , Erskine, F A , and Nalls, W L Streptomycin Sensitivity Development of Sensitivity in Nursing Personnel Through Contact During Administration of the Drug to Patients J A M A **136** 614-615 (Feb 28) 1948

7 Dunner, E Personal communication to the authors

theory of an endocrine or an allergic origin There is, at present, no satisfactory form of treatment other than rest in bed, avoidance of exposure to sunlight and general supportive measures

ABSTRACT OF DISCUSSION

DR ROBERT L GILMAN, Philadelphia This is a remarkable series of cases that Drs Montgomery and McCreight have just reported on It is unusual in the number of patients, the almost exhaustive analyses and the opportunity given for one to compare two consecutive series studied similarly and observed by the same groups The noted differences between the two series are no less surprising than the obvious similarities

I shall not attempt to comment on these worker's histologic studies nor on the findings at autopsy in their variance from those noted by the Mount Sinai group other than to compliment Drs Montgomery and McCreight on their level appraisals, their unwillingness to accept unsubstantiated theories and the avoidance of fanciful conclusions The variation between their findings and those of the Eastern group is not as great as it at first appears the geographic source of their respective patients may be at least one reason for an apparent difference This particular suggestion but recently came to my attention after I had encountered 3 successive cases of acute disseminated lupus erythematosus in young Polish men in Philadelphia The gross morbid changes were of the character and extent described by Baehr and Pollack and Klemperer

It is possible that too much stress has been placed on the importance of collagen or that fibrous tissue structure has been endowed with unproved functions and significance It is known that this structure is of the widest distribution throughout the body, with obvious functions of support, strength and compartmentation Other functions have been concluded However, an increasingly recognized number of disease states characterized by collagen alteration have been grouped together because of these changes, and were this sole common finding the linkage would be tenuous indeed Commoner examples of diffuse collagen diseases, in addition to disseminated lupus erythematosus, are acute rheumatic fever, scleroderma, dermatomyositis and periarteritis nodosa In addition to collagen changes they have other features in common, including the predilection in at least three for persons in the younger age group and for women They diverge greatly in etiologic possibilities—I assume that none of these conditions has a single incontrovertible cause and again this observation is common to all five conditions

Other features that may hold more promise in solving the problem of the causation of disseminated lupus erythematosus are the bone marrow changes, the altered albumin-globulin ratios with the consequent serologic phenomena, and, most recently, the recognition of the "lupus erythematosus" cell It may be in any one of these that we may find the clue to the etiology The observations contained in the charts of the two series of the increasing occurrence of prodromal symptoms, fever, increased sedimentation rates and arthralgia toward the acute phase will add evidence to the ultimate recognition of the cause Parenthetically, it can be added that these same clinical and laboratory signs are sufficiently delineatory to permit the dropping of the qualifying term "arbitrary" from the classification of O'Leary and Madden

I do not believe that one can quite discard the endocrine role in etiology by dismissing with the term "sex predisposition" the overwhelming incidence among younger women Nor can the importance of previous banal infections and the concomitant chemotherapy that appear frequently in the histories of these patients

lesion involving the hands and forearms, worse in the interdigital spaces, and an itching maculopapular lesion involving the circumorbital regions, accompanied with a mild conjunctivitis A second nurse had an intensely pruritic lesion involving all exposed surfaces It was papular, and there were numerous excoriations on the forearms This lesion was definitely aggravated by exposure to sunlight Two exacerbations were produced by the investigators—one by a patch test and the other by twenty minutes' exposure to sunlight The dermatitis cleared in a few weeks, on the patient's avoidance of contact with streptomycin, and at the time of writing, three months after contact with streptomycin was stopped, exposure to sunlight produced no eruption The third patient had a macular eruption on the inner aspects of both forearms and large, itching urticarial patches on the trunk, as well as edema of both upper eyelids These lesions were relieved by treatment with the antihistaminic drugs, cleared when contact with streptomycin ceased and were aggravated by a patch test

SUMMARY AND CONCLUSIONS

Patients receiving streptomycin may acquire a toxic eruption of the skin or mucous membranes There are several varieties a maculopapular erythematous rash, pruritic and self limited, urticaria, exfoliative dermatitis, and stomatitis

These reactions are rare when the daily dose of streptomycin is 1 Gm or less

Exfoliative dermatitis is the only cutaneous eruption which requires cessation of streptomycin therapy

Dermatitis venenata is not uncommon in personnel handling streptomycin regularly over long periods of time It can be avoided by frequent changes in the nursing personnel who come in contact with streptomycin or by having these nurses wear rubber gloves

Veterans Administration Hospital

phalanges and the presence of albumin in her urine Potassium arsenite solution U S P (Fowler's solution) was prescribed because of the persistence of this severe, generalized, pruritic eruption The cutaneous manifestations of dermatitis herpetiformis disappeared almost completely under this medication

In September 1947 the patient exposed herself to sunlight, covering all parts of her body except the upper part of her chest Within a week there developed about a dozen pea-sized to dime-sized, elevated, erythematous lesions of lupus erythematosus on the V area of her chest They remained unchanged for three months

I presented her at the November 1947 meeting of the New York Dermatological Society, at which time she exhibited an eruption of dermatitis herpetiformis undergoing involution, as well as lupus erythematosus

On Dec 8, 1947, she had an extraction of an abscessed tooth, which was followed by fever, malaise and pains in the joints On about March 1, 1948, she presented the typical picture of acute lupus erythematosus of the disseminate type, with all the other classic signs and symptoms accompanying this disease, such as hyperpyrexia, pericarditis and endocarditis

About two or three weeks before her death the eruption of acute lupus erythematosus underwent almost complete involution, and a generalized, malignant, vesicular-bullous-pemphigoid type of erythema multiforme, indistinguishable from Stevens-Johnson disease, as also described by Klauder and later by me, with ophthalmia and oral and genital involvement, assumed the dominant role

The patient died on April 14, 1948 I will not give the details of the post-mortem investigation other than that an anticipated golf-ball-sized remaining accessory spleen was discovered, in addition to pericarditis with organization, pleural effusion and numerous miliary lesions throughout the lungs

Dr George Baehr, who saw this patient, stated that he had seen 3 cases of acute lupus erythematosus of the disseminate type following splenectomy for thrombopenic purpura Did the clinical manifestations, cutaneous and visceral, of this patient all stem from an original infection (probably streptococcic) masquerading in different guises depending on the increasing vulnerability of the host? Was the thrombopenic purpura the first manifestation of her acute lupus erythematosus?

DR WILLIAM H GOECKERMAN, Los Angeles I also had the opportunity to look at Dr Montgomery's paper, and I should like to assure you that the amount of work that it represents is phenomenal Drs Montgomery and O'Leary have had an unusual opportunity in recent years to study this particular subject, and it is a pleasure to hear this paper Many of you know that I have been interested in the subject for a good many years I was glad to hear that Dr Montgomery still emphasizes the general systemic findings, not only in the acute type but also in the subacute form Another point is that he still holds that, histologically as well as clinically, one can see all transitions from the chronic to the acute type To all these points I can heartily subscribe through continued personal study It should again be emphasized that these patients are supersensitive, not only to sunlight, but to all minor interference, including the administration of drugs Small doses in treatment are often much better than larger doses There are many systemic symptoms, including confusing abdominal pains I was extremely glad to hear this paper

DR HARRY ARNOLD JR, Honolulu, Hawaii I should like to suggest that the abdominal pain which sometimes occurs in these patients may have the same cause as that associated with Henoch's purpura abdominalis (nonthrombopenic purpura) and that in differentiation of this pain from that caused by acute surgical lesions of the abdomen it may be helpful to determine the Weltmann coagu-

sarcoidosis The reactions, however, were described as transient, since none of the experimentally induced papules remained palpable for more than eight days No mention was made of a delayed response after the initial inflammatory reaction had worn off, or of any unusual persistence of the experimental lesions—features which are characteristic of the typical Kveim reaction

After the presentation of Kveim's results, other reports appeared which tended to confirm and extend the initial findings [3] These studies indicated that a positive Kveim reaction occurred with a high degree of frequency in patients with sarcoidosis, even when there was no evidence of cutaneous involvement It was suggested, therefore, that the Kveim test might be of considerable value in the diagnosis of the disease, particularly in cases of visceral lesions without extension to the superficial tissues For a number of reasons, however, this possibility has not been realized, and the reaction has remained more a clinical curiosity than a test of diagnostic value

So far as the specificity of the Kveim reaction is concerned, the published data seem to indicate that the cutaneous response is generally limited to patients with sarcoidosis and that positive results in other conditions are uncommon [3e] In exceptional instances, however, a characteristic Kveim response has been observed in certain forms of tuberculosis of the skin, and, with some antigen preparations, positive reactions have been known to occur occasionally in normal persons [3c,d] The latter fact emphasizes the need for testing the specificity of each lot of Kveim antigen on normal controls before using it in a clinical test Even with this precaution the specificity of a given antigen may be difficult to assess, because, like the true positive reaction, a false positive response may require many weeks for its evolution But, as a general rule, most Kveim antigens give positive results only in sarcoidosis and the test is regularly negative in such diseases as syphilis, leprosy, Hodgkin's disease, granuloma annulare, venereal lymphogranuloma, carcinomatosis and tuberculosis [4]

3 (*a*) Danbolt, N On Kveim's Reaction in Boeck's Sarcoid, Acta med Scandinav **114** 143-160, 1943 (*b*) Putkonen, T Ueber die Intrakutanreaktion von Kveim (KvR) bei Lymphogranulomatosis benigna und uber das Bild dieser Krankheit im Lichte der Reaktionsergebnisse, Acta dermat-venereol (supp 10) **23** 1-194, 1943 (*c*) Lomholt, S Beitrag zur Kveimreaktion bei Lymphogranulomatosis benigna, ibid **24** 447-456, 1944 (*d*) Putkonen, T Ueber die Kveimreaktion bei Lymphogranulomatosis benigna, ibid (no 5) **25** 393-410, 1945 (*e*) Danholt, N, and Nilssen, R W Investigations on the Course of Kveim's Reaction and Its Clinical Value, ibid (no 6) **25** 489-502, 1945

4 (*a*) Putkonen [3b] (*b*) Nelson, C T Observations on the Kveim Reaction in Sarcoidosis of the American Negro, J Invest Dermat **10** 15-26, 1948

CUTANEOUS LESIONS OCCURRING IN THE COURSE OF STREPTOMYCIN THERAPY

ARCHIBALD C COHEN, M D
AND
GEORGE C GLINSKY, M D
BUTLER, PA

DERMATITIS in the course of streptomycin therapy was noted by Heilman and associates in 1945 [1] These authors warned that, though such cutaneous lesions do not call for cessation of treatment with streptomycin, it is important for one to be on the alert for severe dermatitis In the report on streptomycin by the National Research Council,[2] 49 cutaneous eruptions were mentioned These were erythematous, urticarial, maculopapular or hemorrhagic Steiner and Fishburn [3] reported 7 cases of rashes occurring during the administration of streptomycin They stated the belief that these reactions are not toxic but allergic In their report to the Council on Pharmacy and Chemistry [4] the Study Units of the Veterans Administration, the Army and the Navy stated that in 18 per cent of 223 cases in which 2 Gm of streptomycin was given daily a pruritic, erythematous, maculopapular skin eruption appeared after about ten days of treatment The pruritus was easily controlled by treatment with diphenhydramine hydrochloride (benadryl hydrochloride®), and the eruption disappeared with continued treatment In 1 4 per cent of the cases in the same series, a severe exfoliative dermatitis appeared

In November 1947 Canizares and Shatin reported the first case of dermatitis venenata due to streptomycin [5] Shortly thereafter, Rauch-

From the Tuberculosis Service, Veterans Administration Hospital

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1 Heilman, D H , Heilman, F R , Hinshaw, H E , Nichols, D R , and Herrell, W E Streptomycin Absorption, Diffusion, Excretion and Toxicity, Am J M Sc **210**.576-584 (Nov) 1945

2 Keefer, C S Streptomycin in the Treatment of Infections, J A M A **132** 70-76 (Sept 14) 1946

3 Steiner, K , and Fishburn, G W Cutaneous Eruptions from Streptomycin, Arch Dermat & Syph **56**.511-516 (Oct) 1947

4 Effects of Streptomycin on Tuberculosis in Man, report of Council on Pharmacy and Chemistry, J A M A **135**·634-641 (Nov 8) 1947

5 Canizares, O , and Shatin, H Dermatitis Venenata Due to Streptomycin, Arch Dermat & Syph **56**·676-677 (Nov) 1947

patients exhibited cutaneous involvement at some time during the course of illness The diagnosis of sarcoidosis in each case was established by microscopic examination of the affected tissue, supplementary confirmation of the diagnosis was obtained by repeated physical examinations, roentgenologic surveys and blood chemical studies Tuberculosis was ruled out by microscopic examination and by cultural studies or inoculation of animals with biopsy specimens

At intervals during the period of observation, efforts were made to estimate the activity of the disease in each patient Sarcoidosis was arbitrarily classified as active when new lesions of the skin, mucous membranes or bones developed, or when there was evidence of progression or persistence of ocular symptoms, hilar adenopathy, infiltration of the parenchyma of the lungs or superficial glandular enlargement All patients in the series were tested intracutaneously with 0 1 cc of various dilutions of old tuberculin U S P, as well as with Kveim antigens and suspensions of normal human spleen in amounts of 0 15 cc

Four Kveim antigens were used during the course of the study Each was a 10 per cent suspension of microscopically proved sarcoid tissue in isotonic sodium chloride solution U S P The suspensions were prepared by the method described by Nelson [4b] and were sterilized by heating in a water bath at 56 C for two hours on each of two successive days Two of the antigens were made

TABLE 1.—*Results of the Kveim Test in Twenty-Four Cases of Sarcoidosis*

State of Disease	Number of Cases	Number of Positive Reactions
Active	15	11
Inactive	9	0
Totals	24	11

from lymph nodes and two from skin The donors were adult Negro patients in the active stages of the disease For testing, 0 15 cc of the antigen was injected intracutaneously through a 22 gage needle into the flexor surface of the forearm The reaction was recorded as positive when a papule occurred at the injection site and remained palpable for at least sixty days from the date of its appearance All persons for whom data are included in the present report were observed at one week to two week intervals for the first ninety days, and more irregularly thereafter, for a minimum period of twelve months Each patient was tested with at least two Kveim antigens before final results were recorded Some received injections of three or four different antigens, the amount of material available did not permit the administration of all four preparations to each patient Whereas the antigens prepared from cutaneous lesions were satisfactory, those made from lymph nodes seemed superior The latter yielded more homogeneous suspensions and, in general, seemed to produce more uniform reactions with less early inflammation than those made from skin

At the time the Kveim test was administered, each patient also was inoculated intracutaneously with two heated 10 per cent suspensions of normal human spleen tissue in isotonic sodium chloride solution U S P The spleen tissue was obtained at autopsy from the bodies of 2 white male patients who had died of cardiovascular disease They had had no obvious infections and had shown no evidence of sarcoidosis The suspensions of spleen tissue were prepared in the same manner as the Kveim antigen, and the criteria for determining the results of the inoculations were the same as those for the Kveim test

a streptomycin patch test was positive, and no other hypersensitivity was demonstrated Urticaria recurred at longer intervals, until finally, six weeks after the cessation of streptomycin therapy, the wheals disappeared permanently The occurrence of urticaria is no reason for the discontinuation of streptomycin therapy

Exfoliative dermatitis is a rare but serious complication of streptomycin therapy Its occurrence is an indication for the immediate withdrawal of streptomycin Only 1 case of this type was seen at this hospital In this case a pruritic maculopapular eruption began after twenty-six days of treatment with streptomycin This eruption persisted until the fortieth day, when exfoliation began, treatment with the drug was promptly stopped, and the skin slowly returned to normal Three weeks later very small doses were tolerated well, but a single therapeutic dose (0 4 Gm) caused an immediate intensely itching maculopapular eruption to appear all over the patient's body Pruritus was most pronounced on the chest and upper extremities Treatment with the drug was at once stopped Several days later, the skin all over the body began to shed fine scales, while large areas of skin sloughed from the hands and feet Each eruption was accompanied by eosinophilia, with a count of from 15 to 20 per cent, neither the itching nor the scaling was benefited by treatment with antihistaminic drugs In most cases of exfoliative dermatitis reported by others, no previous benign rash existed

In 2 instances the lips became dry and chapped, with fissuring and considerable soreness In both cases the patients were receiving 2 Gm of streptomycin daily, neither had eosinophilia, and neither was benefited by treatment with antihistaminic drugs In both cases a degree of relief could be obtained by the use of bland ointments This complication does not require the cessation of streptomycin therapy

In 1 case the tongue became swollen, red and painful, with superficial ulceration covered with a yellowish membrane This patient also was receiving 2 Gm of streptomycin daily There was moderate discomfort, but it was possible to continue treatment

Three cases of dermatitis venenata were seen in nurses who had used streptomycin regularly over a long period of time One case arose after six weeks of exposure, and the others, after three months No cases were seen in personnel with limited exposure to streptomycin In all these 3 cases reactions to patch testing were positive In 2 cases the patch test was accompanied with a flare-up of the entire lesion, which exacerbation subsided in two or three days In all cases the lesions subsided when contact with the drug was stopped in 1 instance by the nurse's being moved to a ward where the drug was not used and in the others by the wearing of rubber gloves The lesions themselves were quite different in the 3 cases One nurse had an itching vesicular

It is also not clear whether all suspensions of material from normal human spleens are capable of producing the Kveim response in patients with sarcoidosis As is true of Kveim antigens prepared from sarcoid tissue, suspensions of normal human spleen apparently may also vary considerably in their capacity for inducing the sarcoid response

RESULTS

The data in table 1 show that the Kveim reaction was positive in 11 of the 15 patients with active sarcoidosis In none of the 9 patients with healed or



Fig 2—Extensive production of sarcoid-like tissue seven months after the intracutaneous administration of a suspension of normal human spleen Note naked tuberculoid structure, with occasional giant cells of the Langhans type Hematoxylin and eosin stain, × 100

inactive sarcoidosis was a positive reaction obtained These results indicate that negative Kveim reactions may be expected in a significant number of patients even with the clinically active stages of sarcoidosis, and that, consequently, the test can be of only limited diagnostic value However, it is possible that the reaction may be of some help in anticipating the course of the disease, since

KVEIM REACTION IN SARCOIDOSIS

CARL T NELSON, M D
NEW YORK

CONSIDERABLE interest has recently been aroused by Kveim's report [1] of the production of an unusual cutaneous reaction in patients with sarcoidosis by the intracutaneous injection of heated saline suspensions of tissue obtained from persons with active disease Kveim found that after the transient inflammatory response caused by the trauma of such an injection had subsided, a small, indurated papule developed at the test site within a variable period of time This delayed papular reaction was distinctive in that it often required weeks to attain its maximum size and usually remained visible for many months thereafter Microscopic examination of tissue from sites of such reactions showed a histologic structure essentially the same as that of the lesions of the natural disease Since control injections of Frei antigen and old tuberculin injected simultaneously with the suspensions of tissue into the same patients produced no comparable response, and, since the sarcoid material yielded negative results when injected intracutaneously into normal persons or persons with syphilis or lupus vulgaris, Kveim concluded that the cutaneous reaction was specific for sarcoidosis He also postulated that the cutaneous response was based on an allergic mechanism, although no experimental support for that contention was presented

Several years prior to the publication of these results, Williams and Nickerson [2] described a cutaneous reaction in sarcoidosis which, in retrospect, appears similar in some details to that reported by Kveim These investigators, using an antigen of sarcoid tissue prepared in a manner nearly identical with that subsequently employed by Kveim, produced cutaneous reactions by intracutaneous injection in 4 cases of

From the Department of Dermatology, Columbia University College of Physicians and Surgeons, and the Vanderbilt Clinic, Presbyterian Hospital

Read before the Section on Dermatology and Syphilology at the Ninety-Seventh Annual Session of the American Medical Association, Chicago, June 23, 1948

1 Kveim, A Preliminary Report on New and Specific Cutaneous Reaction in Boeck's Sarcoid, Nord med **9**.169-172, 1941

2 Williams, R H, and Nickerson, D A Skin Reactions in Sarcoid, Proc Soc Exper Biol & Med **33** 403-405, 1935

reactions to cutaneous tests with the various clinical manifestations of sarcoidosis, or with the degree of sensitivity exhibited by these patients to old tuberculin U S P, were unsuccessful While the number of cases in the present series is too small to

TABLE 3.—*Sites of Previous Lesions and Results of Kveim and Other Intracutaneous Tests in N*
Cases of Healed or Inactive Sarcoidosis

				Sites of Lesions During Active Phases of Disease									Results of Intracutaneous Tests			
														Old Tuberculin U S P		
Case Number	Age, Years	Sex	Months of Remission	Skin	Hilar Lymph Nodes and/or Lung	Superficial Lymph Nodes	Salivary or Lacrimal Glands	Bone	Eye	Other*	Kveim†	Spleen Suspensions‡	1 mg	0.1 mg	0.01 mg	0.001 mg
16	37	F	26	+	+	+	0	0	0	+	0	0		+	0	0
17	26	F	17	+	+	0	0	0	0	0	0	0		+	+	0
18	42	F	28	+	±	0	0	0	0	0	0	0	+	±	0	0
19	54	F	53	0	+	+	+	±	+	+	0	0		+	0	0
20	34	F	29	0	+	+	0	0	0	+	0	0		+	0	0
21	40	F	104	+	+	0	0	+	0	+	0	0		+	+	+
22	58	F	46	+	+	+	0	+	0	+	0	0		+	0	0
23	39	F	61	+	0	+	0	0	0	0	0	0		+	0	
24	34	F	40	+	+	0	±	0	+	0	0	0		+	0	0

+ = Present or positive, ± = equivocal, 0 = absent or negative
* Cases 16, 21 and 22, mucous membrane, case 19, palpable liver, case 20, palpable liver and spleen
† Results obtained with two or more antigens
‡ Results obtained with two suspensions of human spleen

TABLE 4.—*Serum Values in Fifteen Cases of Active and Nine Cases of Inactive Sarcoidosis*

	Laboratory Observations							
Classification and Case Number	Total Proteins, Gm per 100 Cc	Albumin, Gm per 100 Cc	Globulin, Gm per 100 Cc	Alkaline Phosphatase, Bodansky Units per 100 Cc	Cephalin Flocculation (48 Hr.)	Calcium, Mg per 100 Cc	Inorganic, Phosphorus, Mg per 100 Cc	Total Cholesterol, Mg per 100 Cc
Active sarcoidosis				Kveim Positive				
1	8.2	3.7	4.5	7.0	0	8.8	4.1	175
2	7.3	4.5	2.8	1.8	++		4.4	192
3	7.4	4.7	2.7	5.9	±	9.3		247
4	8.1	4.4	3.8	10.1	0	10.2	3.1	149
5	7.4	3.9	3.5	5.9	++		3.4	250
6	7.8	3.9	3.9	3.3	0	10.0		265
7	7.5	4.2	3.3	2.5	0	9.6	3.2	246
8	7.5	4.9	2.6	1.9	0	9.9		
9	6.9	4.2	2.7	1.6		10.3	4.1	208
10	8.4	4.2	4.2	5.8	++	11.0	4.3	179
11	6.8	4.2	2.6	3.2	++	10.4	3.7	204
				Kveim Negative				
12	7.3	3.8	3.5	2.8	±	10.1	3.8	
13	9.4	4.1	5.3	6.4	++	10.7		260
14	8.4	4.1	4.3	3.6	+++	9.8	3.8	222
15	7.1	3.5	3.6	2.5	0	11.0	4.6	
Inactive sarcoidosis				Kveim Negative				
16	8.0	4.5	3.5	14.4	0		3.6	234
17	7.2	4.6	2.6	3.3		10.8	3.2	
18	7.7	4.2	3.5	4.2	0	10.3	3.7	165
19	7.3	5.1	2.2	5.0	+	10.6	4.8	
20	8.3	4.7	3.6	6.9	++	9.7	3.1	199
21	9.0	3.7	5.3	3.3	0	11.8		167
22	8.1	5.0	3.1	2.0		10.8	3.9	321
23	6.8	3.3	3.5	1.9	+		4.0	
24	7.7	4.7	3.0	3.5	0	10.0	3.9	142

permit definite conclusions, the data presented in tables 2 and 3 do not suggest that the capacity for characteristic cutaneous reactions to Kveim antigens and suspensions of normal human spleen is associated with any particular type or degree of sarcoidosis As might have been expected, the patients with the inac-

In another sense, however, there is considerable evidence that the Kveim reaction, rather than being a specific phenomenon, may be only a general cutaneous response on the part of persons with sarcoidosis to a number of different substances For example, it has been shown that a reaction similar to that described by Kveim may sometimes be observed in cases of sarcoidosis after the intracutaneous injection of saline suspensions of leukemic human lymph nodes [3d] or killed tubercle bacilli [5] More recently, it has been observed that patients who exhibit a positive cutaneous reaction to the injection of Kveim antigen prepared from sarcoid material may also give a typical Kveim response to the intracutaneous administration of suspensions of normal human spleen pulp [4b] In these cases, biopsy specimens obtained from the site of injection of human spleen pulp after a period of several months often showed a histologic picture similar to that of a spontaneous sarcoid and fairly comparable to that induced by injections of Kveim antigen derived from sarcoid tissue Thus, although the specificity of the Kveim reaction is such that the cutaneous response is usually limited to patients with sarcoidosis, the fact that such persons often react in an identical fashion to the intracutaneous administration of normal human spleen tissue, and sometimes of leukemic lymph nodes and tubercle bacilli, strongly suggests that the response does not depend on any specificity inherent in the sarcoid tissue used in the preparation of the antigen Instead, such evidence indicates that the Kveim reaction as seen in patients with sarcoidosis may be only an unusual isomorphic response to one or more chemical complexes, present in certain human tissues and in other substances

During the two years previous to this report, an opportunity to study the characteristics and possible clinical significance of the Kveim phenomenon was afforded by the presence of a group of 24 persons with proved sarcoidosis These patients provided further data on certain features of the reaction, the intent of this report is to summarize the results of this experience to the time of writing

MATERIALS AND METHODS

The cases of sarcoidosis included in this study were chosen at random from those of outpatients and patients admitted to the hospital with this disease Twenty-one patients were Negroes and 3 were white In most instances the chief manifestations were dermatologic, but in some the presenting symptoms were predominantly those of generalized sarcoidosis Nevertheless, all but 4 of the

5 (*a*) Lemming, R Development of Boeck's Sarcoid at the Place on the Skin Where a BCG Vaccination Had Been Made in a Case of Schaumann's Disease Acta med Scandinav **110** 151-160, 1942 (*b*) Warfvinge, L E Boeck's Sarcoid Experimentally Produced by Virulent, Human Tubercle Bacilli in a Case of Schaumann's Disease ibid **114** 259-270, 1943

The exact nature of the chemical complexes which are capable of artificially inducing these sarcoid-like tissue reactions has not been determined There is evidence that some, at least, are relatively heat stable It has been shown that Kveim antigens can withstand boiling for twenty minutes without loss of reactivity [3d] Other preliminary studies suggest that the active principles in normal human spleen tissue are associated in some way with the lipid fractions [6] But whatever the chemical nature of the agents responsible for the unusual tissue reactions in question may be, it is clear that the agents can produce sarcoid responses only when injected in grossly particulate form Berkefeld filtrates of Kveim antigen or suspensions of normal human spleen do not induce the characteristic cutaneous reactions Thus, the Kveim response and other similar phenomena observed in patients with sarcoidosis seem to depend not only on the chemical makeup of the materials injected but also on the size of the particles Unless the particles of injected material can serve as localized depots of stimulation for relatively long periods of time, the typical cutaneous reactions will not ensue Some investigators [8] have suggested that the Kveim response is an allergic phenomenon If this is true it is difficult to explain the delayed appearance of the reaction, unless one postulates that a prolonged latent period is needed before the sensitized tissue can react with the immobilized aggregates of antigen Evidence for this is lacking, however, and for the present it may be just as fruitful merely to regard the Kveim reaction as a general tissue response on the part of patients with sarcoidosis to a chemical foreign body

Attempts to employ the Kveim reaction in the diagnosis of sarcoidosis have not been particularly successful The antigens used thus far not only have been relatively crude and difficult to standardize but also have had the disadvantage of producing extremely persistent nodular lesions in positive reactors Sometimes these lesions become necrotic and form disfiguring ulcers, which may require many months to heal [3c, d] In addition, although false positive reactions are uncommon, a certain number of patients with active disease apparently do not respond to the test Even when the reaction is positive, it may be so delayed in its evolution that it loses much of its practical diagnostic significance On the other hand, there is some evidence that the test may be of occasional prognostic value in following the course of the disease, since in some instances the Kveim reaction has involuted completely at the time when the patient began to show evidence of clinical remission Aside from this apparent association with the activity of the disease the Kveim response does not seem to have any obvious relation to the type or degree of clinical involvement, or to the characteristic changes in certain blood values in patients with sarcoidosis

8 Kveim [1] Danbolt [3a]

The sarcoid antigens and suspensions of normal human spleen tissue employed in this study did not produce the characteristic delayed papular reaction when injected intracutaneously into normal persons, or into patients with diseases other than sarcoidosis A certain amount of early inflammation occurred at the injection sites in all persons after the administration of these substances, but in the sarcoid-free controls this reaction was evanescent and disappeared within two or three weeks Subsequent investigations, using material from a number of different



Fig 1—Sarcoid-like response ten months after the intracutaneous injection of Kveim antigen The cells infiltrating the lesion are epithelioid cells and lymphocytes Giant cells were rare Hematoxylin and eosin stain, × 100

normal human spleens, have shown that some suspensions of spleen tissue may lose their specificity after several months of storage and produce persistent papular lesions in nearly all persons after intracutaneous injection[6] The reason for this phenomenon is not known, but it again emphasizes the need for frequent evaluation of the specificity of such products before their use in tests of this sort

6 Nelson, C T Unpublished data

coidosis, clinically characteristic and histologically proved Intracutaneous tests were made and the patients watched over a long period However, no reaction developed at the injection site in any of the patients Three of the patients had a regressing stage of the disease when they were tested This would corroborate Dr Nelson's finding of reduced positivity or complete negativity in similar cases when the active process was on the wane However, he reported negative Kveim reactions when patients in active stages of the disease were tested with old antigens This again may be a factor in our failure to obtain positive reactions, because the antigen which we used was at least six months old

Furthermore, we prepared an antigen with tissue obtained from a patient whose condition was definitely improving When the material was used in testing persons who manifested active sarcoid disease, the results were negative I should like to ask Dr Nelson if he has had a similar experience I should like to say one additional thing regarding sarcoid-like tissue reactions in general Lately I observed a patient who had been working beneath a fluorescent light when it fell and broke, lacerating the dorsum of her hand Early healing progressed uneventfully, but, when closure was almost complete, several small papules developed about the edges of the injured site Biopsy sections revealed beryllium particles, I regarded the particles as causative of the tissue reaction shown

Dr Bernard Appel, Lynn, Mass It is useful for Dr Nelson to have revived this particular subject, especially because some contradictory statements have been made, particularly in regard to the specificity of the test At the Boston City Hospital, in the dermatology department, this test has been performed since 1934, which, incidentally, was a long time before Kveim did his work In Boston, Donald A Nickerson and R H Williams, back in 1932, conceived the idea that sarcoidosis or sarcoid-like lesions might produce a specific virus type reaction similar to that in venereal lymphogranuloma They removed sections from lesions, ground them up, made a sterile suspension, performed tests and reported their observations [2]

The question is What about the specificity of this test? It appears to me that it is specific The mere fact that a patient with sarcoidosis or a patient with sarcoid-like lesions also reacts to an injection of tuberculin or spleen tissue does not necessarily mean that this particular test is nonspecific After hearing this excellent presentation, my impression is that a pretty good case has been made out for its specificity I would not go any further than the author of the paper in proposing it as an absolute, iron-clad test, but I think pursuit of the subject should lead to still more knowledge The corollary of the statement that patients whose disease is in remission do not exhibit the positive Kveim response is that periodic retesting of patients with active, progressive symptoms of the disease ought to give a fairly reasonable picture of the possibility of prognosis and of the development of the disease

Another interesting phenomenon, which Kveim himself noted in his paper in 1941, was that the latent interval which elapsed between the inoculation and the development of the nodule grew progressively shorter and shorter as the disease progressed in its intensity The implications of that observation should be studied further I want to take this opportunity again to protest against eponymic nomenclature I do not see what is gained by hitching a man's name onto a test like this Let us instead call it an intradermal skin test for sarcoidosis, scientific progress is thus better served Eponyms have only historical value and cater to vanity

reactions in the patients in whom the disease was in remission were all negative Further evidence of the value of the test in prognosis is the result noted in 4 persons with active sarcoidosis in whom the disease entered a phase of clinical remission during the period of study In 2 of these patients, reactions to repeated Kveim tests were negative from the beginning of observation After six months and seven months, respectively, the clinical signs of sarcoidosis subsided rather rapidly, and both patients subsequently remained asymptomatic In the 2 other patients clinical remission occurred ten months and thirteen months, respectively, after the start of observation In both instances, the Kveim reaction was originally positive, but the experimental lesions began to involute as the patients approached the stage of clinical improvement Thereafter, reactions to repeated Kveim tests in these patients were negative, despite the fact that the reactions had previously been positive

TABLE 2.—*Various Clinical Manifestations and Results of the Kveim and Other Intracutaneous Tests in Fifteen Patients with Active Sarcoidosis*

				Sites of Lesions							Results of Intracutaneous Tests				
												Old Tuberculin U S P			
Case Number	Age, Years	Sex	Months Since Onset of Disease	Skin	Hilar Lymph Nodes and/or Lung	Superficial Lymph Nodes	Salivary or Lacrimal Glands	Bone	Eye	Other*	Kveim†	Spleen Suspensions‡	1 mg	0.1 mg	0.01 mg	0.001 mg
1	34	F	99	0	±	+	+	0	+	+	+	+	0	0	0	0
2	44	F	82	+	+	±	+	0	+	+	+	+	0	0		
3	41	F	56	+	±	+	0	0	0	+	+	+	±	0	0	
4	31	M	63	+	±	+	0	0	0	+	+	+	0	0	0	
5	50	M	73	+	+	+	0	0	0	±	+	+	+	0	0	0
6	43	F	24	+	+	±	0	0	0	0	+	+	±	0	0	
7	32	F	34	+	+	0	0	0	0	+	+	+	0	0	0	
8	40	F	37	+	+	±	0	0	0	0	+	+		+	0	0
9	40	F	22	+	0	0	0	0	0	0	+	+	0	0	0	0
10	32	M	37	+	+	+	0	+	0	0	+	+	0	0	0	
11	36	F	18	+	+	0	+	0	0	0	+	+	+	±	0	0
12	40	F	25	0	0	+	0	0	0	0	0	0	±	0	0	
13	26	F	22	+	+	±	0	0	0	+	0	0	0	0	0	0
14	24	F	35	+	0	+	0	0	0	+	0	0	0	0	0	
15	24	F	13	+	0	+	+	0	0	+	0	0	0	0	0	

+ = Present or positive, ± = equivocal, 0 = absent or negative
* Case 1, coincidental weakness of facial nerve, case 2, tonsils, cases 3, 4 and 7, mucous membrane, cases 5, 13 and 14, palpable spleen, case 15, palpable liver
† Results obtained with two or more antigens
‡ Results obtained with two suspensions of human spleen

Thus, in this group of patients, 9 persons in whom sarcoidosis was already inactive gave negative Kveim reactions, 4 others, who were about to show clinical remission, showed negative reactions either at that point or as the disease began to subside These data suggest that the test, although it may not be much help in the diagnosis of sarcoidosis, may be of some use in judging the prognosis in a case at hand If reactions to successive Kveim tests remain persistently positive in a case of active disease, the probability is that clinical improvement is still some time away

It is of interest that the patients who showed a positive cutaneous reaction to the injection of sarcoid material without exception also presented a typical Kveim response to the intracutaneous injection of normal human spleen tissue Biopsy specimens taken from the sites of both tests after a period of six to ten months showed a histologic picture comparable to that of a spontaneous sarcoid (figs 1 and 2) Attempts to correlate the development of these characteristic

DISSEMINATED AND CIRCUMSCRIBED NEURODERMATITIS TREATED WITH PHENINDAMINE (THEPHORIN®)

WILFRED E WOOLDRIDGE, M D *
SPRINGFIELD, MO
AND
HERBERT L JOSEPH, M D
Resident in Dermatology
ST LOUIS

IN 1910 Dale and Laidlaw [1] advanced the hypothesis that histamine or histamine-like bodies were the chemical compounds responsible for the phenomena of anaphylaxis Since that time numerous investigators have produced evidence which seems to confirm that original idea, and the hypothesis has been extended to explain all or most of the phenomena associated with allergy in the broadest sense

Diphenhydramine hydrochloride (benadryl hydrochloride®) and tripelennamine hydrochloride (pyribenzamine hydrochloride®) were the first drugs available in this country which seemed to play the role of "antihistaminic" agents, although they were preceded in Europe by numerous other preparations Chemists have been and are still trying to find an ideal drug which (1) will have little or no side effects and (2) will produce better effects through penetration of the skin

However strong the evidence may seem, histamine has never been proved entirely responsible for all the allergic manifestations attributed to it Notable has been the failure of histaminase, an enzyme shown to be capable of inactivating histamine but disappointing when applied clinically Also must be considered the failure of the "antihistaminic" drugs to inactivate histamine in vitro and the lack of any but circumstantial evidence that such inactivation occurs in vivo At any rate, histamine is apparently not initially involved in the process which leads to anaphylaxis or allergic manifestations, for there first occurs an antigen-antibody reaction resulting in cell injury At that point histamine first enters the picture, either being a direct product of the antigen-antibody reaction

*Formerly Research Assistant in Dermatology, Barnard Free Skin and Cancer Hospital, St Louis

Studies, observations and reports from the Department of Dermatology of the Barnard Free Skin and Cancer Hospital and Washington University School of Medicine, service of Dr Richard S Weiss

1 Dale, H H, and Laidlaw, P R The Physiological Action of Beta-Iminazolylethylamine, J Physiol **41** 318-344, 1911

tive stage of the disease showed a generally higher level of reactivity to old tuberculin than did those with active sarcoidosis Although slight variations in sensitivity to tuberculin occurred in persons with active sarcoidosis, the variations seemed to bear no obvious relation to the ability or inability of the persons to react to suspensions of human spleen and sarcoid tissue

A number of laboratory studies were also undertaken in the cases of this series to learn whether the presence of a cutaneous response to injections of sarcoid material and human spleen tissue might be related in some way to variations in the values for certain constituents of the blood The results of these observations are summarized in table 4 The values are those obtained at the time the cutaneous tests were administered It is evident from these data that there was no clearcut relation between the various blood values in sarcoidosis and the cutaneous reaction to Kveim antigen and suspensions of human spleen

COMMENT

It seems apparent from the studies presented in this report and elsewhere [7] that many persons with clinical sarcoidosis respond in a typical manner to the intracutaneous administration of various organic materials After such injections, delayed papular reactions, having a histologic structure comparable to that of a spontaneous sarcoid, often develop at the test sites Responses of this sort may be produced with some regularity with injections of heated saline suspensions of sarcoid tissue, normal human spleen pulp, leukemic lymph nodes and tubercle bacilli On the other hand, intracutaneous injections of saline suspensions of calcium sulfate, collodion particles, coagulated egg white, Pityrosporum ovale, defatted human skeletal muscle, normal human lymph nodes and oil-free soybean phosphatides do not result in such reactions [4b]

It has been known for many years that lesions having the microscopic anatomy of typical sarcoids can sometimes be produced experimentally by the injection of certain oils, as well as lipid-containing extracts of various bacteria Moreover, it is also well established that local histologic changes comparable to those seen in sarcoidosis may be found in such conditions as tuberculoid leprosy, syphilis, tuberculosis, leishmaniasis, brucellosis, chronic beryllium poisoning and certain fungous infections These facts are only suggestive, but they lend some support to the viewpoint, shared by many investigators, that the tissue reactions in sarcoidosis are not in themselves specific but merely represent a general histologic response to a number of different agents With this possibility in mind, it is perhaps understandable that certain persons with active sarcoidosis who seem to possess this general type of tissue reactivity to a considerable degree should respond in a similar fashion to the injection of several seemingly different substances

7 Kveim [1] Danbolt [3a] Putkonen [3b] Lomholt [3c] Putkonen [3d] Danbolt and Nilssen [3e] Nelson [4b] Lemming [5a] Warfvinge [5b]

and these drugs, together with the remaining commercial antihistaminic compounds, except for phenindamine, are derivatives of the older Forneau compounds As indicated previously, phenindamine, which to date is chemically unique and distinct from the others now available, is not

The phenindamine base has a melting point of 90 to 91 C The salts of the base which are employed clinically melt at considerably higher temperatures At room temperature the tartrate salt is soluble, up to 3 per cent, in water A 2 per cent aqueous solution has a *p*H of 5

PHARMACOLOGY

Toxicity studies have revealed that phenindamine shows approximately the same degree of toxicity to animals as does diphenhydramine

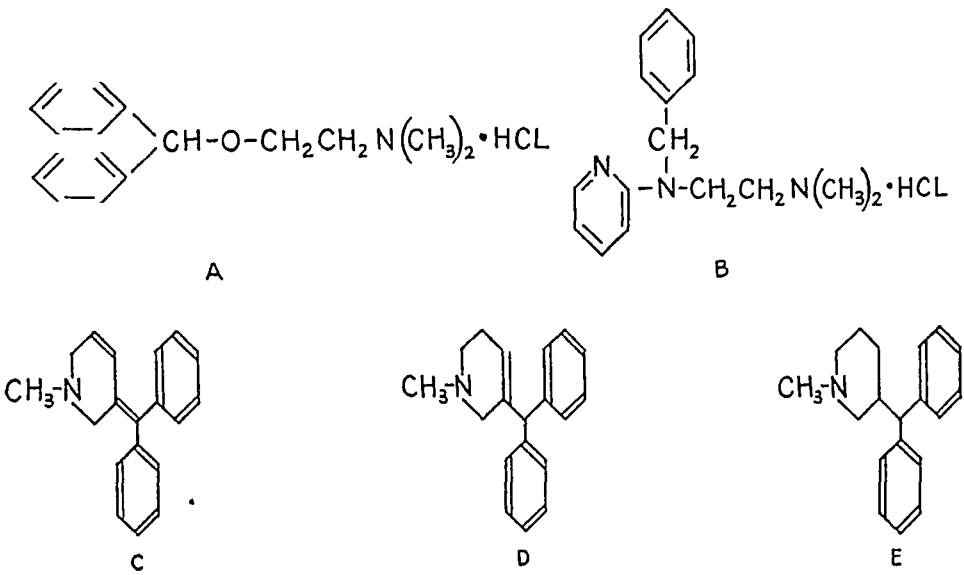


Fig 1—Structural formulas for diphenhydramine hydrochloride (*A*), tripelennamine hydrochloride (*B*), Nu-1326 (*C*), Nu-1504, or phenindamine (*D*) and Nu-1525 (*E*)

hydrochloride but considerably less than does tripelennamine hydrochloride Guinea pig protection experiments against a histamine spray showed a more favorable milligram per kilogram protection with phenindamine than with diphenhydramine hydrochloride but less with phenindamine than with tripelennamine hydrochloride In man it was shown that the size of histamine wheals was moderately reduced when phenindamine was taken by mouth and also that the erythema was much less and itching completely absent in 5 of 6 subjects Lehmann [4] showed

4 Lehmann, G Pharmacological Properties of a New Antihistaminic 2-Methyl-9-Phenyl-2,3,4,9-Tetrahydro-1-Pyridindene (Thephorin) and Derivatives J Pharmacol & Exper Therap **92** 249-259 (March) 1948

SUMMARY

1 In a study of the Kveim phenomenon in 24 cases of sarcoidosis the reaction was positive in 11 of 15 patients with active disease In none of the 9 cases of healed or inactive sarcoidosis in the group was a positive Kveim response obtained

2 All persons who showed a positive cutaneous reaction to the injection of Kveim antigen also showed a typical sarcoid-like response to the intracutaneous injection of suspensions of normal human spleen tissue

3 The capacity for these characteristic cutaneous reactions did not seem to have any consistent relation to the type of clinical involvement, to the degree of sensitivity to tuberculin or to changes in the values for certain blood constituents observed in sarcoidosis

4 Although the Kveim reaction is of little value in the diagnosis of sarcoidosis, there is some evidence that it may be of occasional prognostic use in following the course of the disease

630 West One Hundred and Sixty-Eighth Street (32)

ABSTRACT OF DISCUSSION

DR MAX MICHAEL, Chamblee, Ga This so-called Kveim reaction is indeed unique The long latency for its development, sometimes as long as eighteen months before it becomes positive, would certainly remove it from the group of intracutaneous reactions such as the immediate anaphylactic reaction or the delayed tuberculin type reaction

Dr Nelson has wisely stressed the complete nonspecificity of the reaction One should call to mind the number of cases in which sarcoid lesions have been reported after trauma One cannot say that these patients have sarcoidosis, but rather that sarcoid lesions developed after trauma in which bits of silica or sand were apparently driven into the skin This view would suggest that the Kveim reaction and the type of reaction which appears after trauma with silica represent the capacity of the patient to react to certain foreign, extraneous materials, as Dr Nelson has emphasized

It seems that the usefulness of the Kveim reaction will lie not in its diagnostic value and perhaps not so much in its prognostic value, but probably in its being just another tool with which we can study the pathogenesis of disease

If one could find out exactly what brings about the Kveim reaction, and the chemical fractionation of the tissue responsible for it, then one could better understand the whole mechanism and pathogenesis of sarcoidosis

I should like to ask Dr Nelson two questions concerning results using the various fractions First, is the histologic structure comparable to that seen with the sarcoid tissue? Secondly, does the reaction appear in a length of time shorter than that when the whole tissue extract is used?

DR JOHN DALTON, Indianapolis The workers at Indianapolis General Hospital have been pursuing studies on the Kveim reaction I should like to report on our work because this presentation clarifies some of our confusing results Dr Morris Leider provided us with some Kveim antigen which he had received from Dr Putkonen The amount was small We selected 6 patients with sar-

irritation during use of the ointment were given patch tests with the complete ointment and also with the ointment base

Results of Treatment—As will be seen from the data recorded in tables 1 and 2, the treatment of disseminated neurodermatitis met with more success than did the treatment of circumscribed neurodermatitis



Fig 2—Photomicrograph of skin from the right antecubital space of patient (D S) with severe disseminated neurodermatitis, before treatment (× 115)

Disseminated Neurodermatitis—It was encouraging to note that many of the patients with disseminated neurodermatitis insisted on the continuation of this treatment because it gave the only significant relief they had ever received from therapy other than roentgen rays It will be noted from table 1 that only 2 of the 23 patients had complete

DR MAURICE OPPENHEIM, Chicago I wish to make only a short remark about the sarcoid reaction of the skin in general About twenty-five years ago I reported several cases of localized sarcoids or lipid reactions in sites where subcutaneous injections had been made with soluble and insoluble drugs, like suspensions of mercury or bismuth in oil Later, Volk performed experiments in which he was able to produce sarcoids by subcutaneous injections of india ink This shows, as Dr Nelson and the other speakers pointed out, that the sarcoid reaction may be a specific reaction of the skin This reaction should not be confused with the foreign body reaction, which is histologically different In an excellent paper on sarcoidosis, which Dr Michelson read a year ago in Atlantic City, he mentioned my data

DR CARL T NELSON, New York Dr Michael's suggestion that the injection of silica-containing material may produce a sarcoid-like response, comparable to that induced by the Kveim antigen, is well taken Tissue reactions to silica can mimic the Kveim reaction in almost every detail, that is why sand must not be used for grinding the tissue during the preparation of antigen suspensions of this sort

A clarification of the mechanism of the Kveim response might be helpful in explaining the pathogenesis of naturally occurring sarcoid lesions At present, little is known about the chemical makeup of the substances which can provoke the Kveim type of reaction Recently, I have tried to isolate the active fractions which are known to be present in at least some normal spleens I have not been successful thus far, but there is evidence that the active principles are linked with compounds of a lipid nature

As Dr Dalton has indicated, antigens prepared from different specimens of sarcoid tissue may vary greatly in their ability to produce the Kveim response The period during which an antigen will retain its reactivity also seems subject to considerable variation However, I am not in a position to comment on this point, since my woefully small supplies of antigen have always been used up in a few months

The occurrence of localized sarcoid granulomas in persons who have cut themselves on broken fluorescent lamps coated with beryllium phosphor is very interesting The histology of these traumatic lesions is similar to that in spontaneous sarcoids and to that in the cutaneous lesions of workers in whom pulmonary granulomatosis has developed after exposure to beryllium

In reply to Dr Appel, let me emphasize that the Kveim reaction is specific in the sense that it is usually limited to persons with active sarcoidosis Positive responses in other diseases are uncommon On the other hand, the reaction is nonspecific in the sense that a similar response may be elicited in patients with sarcoid after the administration of substances other than sarcoid tissue In other words, the Kveim response does not depend on any specificity inherent in the tissue used in the antigen Sometimes suspensions of tubercle bacilli or normal spleen tissue will do as well

In my experience, the performance of repeated Kveim tests over a period of months in cases of active sarcoidosis has not shortened the time required for a positive reaction This might be taken as evidence against the theory that the reaction depends on an allergic mechanism If it did, one might expect acceleration of the response under these circumstances

Dr Oppenheim may be correct in considering the Kveim reaction to be primarily a foreign body response Apparently he has been able to produce sarcoid like lesions with many more substances than I

any such history Likewise, we could not correlate the amount of improvement with the degree of involvement

With most of our patients the relief of itching was dramatic after the first application of the ointment Relief occurred within fifteen minutes and usually lasted two to three hours or longer There was



Fig 4—Photograph of forearms of control patient (J R) with severe, generalized disseminated neurodermatitis of many years' duration, taken after one week of local treatment with phenindamine phosphate ointment to the left arm and application of ointment base only to the right arm

occasionally reported a very brief smarting, which occurred in weeping areas immediately after application of the ointment In practically all cases the itching was so relieved that the patients no longer scratched, and in many cases itching was no longer present at all

or being released by the injured cells It is evident, therefore, that "antihistaminic" drugs probably play no part in preventing the anaphylactic or allergic reaction but rather prevent, in a still unrecognized way, the clinical manifestations which are recognized

If these theories are correct, the "antihistaminic" drugs are at once relegated to the position of stopgaps in therapy, for they do not prevent the allergic reaction but only modify it This contention is borne out by the many examples in which hay fever or urticaria, for example, is controlled for long periods only to have the patient suffer a relapse when use of the "antihistaminic" drugs is discontinued However, the success with which these drugs are employed has resulted in a discouraging tendency for all attempts at discovery of offending agents to cease

It is now known that the "antihistaminic" drugs may accomplish some of their actions without histamine being involved at all That this statement is clearly true will be subsequently indicated by our studies and is already shown with regard to the anesthetic action of these drugs as related by Friedlander and Feinberg [2] Also, the sedative action of these drugs is well known and seems to be entirely separate from their properties as histamine antagonists

This paper reports the use of a new drug, phenindamine (thephorin®), which must be included in the group of drugs used in the symptomatic relief of allergic disease [3]

CHEMISTRY

Phenindamine not only is a different antihistaminic agent but belongs to an entirely new and heretofore unknown series of compounds It is a polycyclic amine, the empiric formula of which is $C_{16}H_{19}N$ (2-methyl-9-phenyl-2, 3, 4, 9-tetrahydro-1-pyridindene) Of this series of compounds only phenindamine has shown significant antihistaminic activity The structural formulas of two others of this series, differing from phenindamine only by the position of their double bonds, are shown in figure 1 and are considered briefly in this paper The structural formulas for diphenhydramine hydrochloride (beta-dimethylaminoethyl benzohydryl ether hydrochloride) and for tripelennamine hydrochloride (N, N - dimethyl - N'- benzyl - N'- [α - pyridyl] ethylenediamine hydrochloride) are shown for comparison The similarity between diphenhydramine hydrochloride and tripelennamine hydrochloride may be seen,

2 Friedlander, S, and Feinberg, S Histamine Antagonists III The Effect of Oral and Local Use of Beta-Dimethyl-Amino-Ethyl Benzhydryl Ether Hydrochloride on the Wheaing Due to Histamine, Antigen-Antibody Reactions, and Other Wheaing Mechanisms Therapeutic Results in Allergic Manifestations, J Allergy **17** 129-141 (May) 1946

3 All materials for this study were supplied by Hoffmann-La Roche, Inc, Nutley, N J

TABLE 1—*Data on the Treatment with Phenindamine of Patients with Disseminated Neurodermatitis*

Patients Treated with Phenindamine

Patient	Age	Degree of Eruption	Duration of Eruption	Regions Affected (Bilaterally)	Length of Treatment	Results of Treatment in Percentages of Improvement		Reactions
						Subjective	Obective	
D S	11 yr	Severe	10 yr	Eyelids, neck, wrists, popliteal and antecu bital fossae	3 wk *	More than 75%	More than 50%	None
J S	15 yr	Severe	15 yr	Eyelids, neck, wrists, popliteal and antecu bital fossae	7 wk *	More than 75%	More than 50%	None
L C	16 mo	Moderate	15 mo	Antecubital and popli teal fossae	1 wk *	More than 50%	More than 50%	Insomnia
D D	2 yr	Mild	22 mo	Antecubital and popli teal fossae	3 wk *	100%	100%	Insomnia, irritability
D H	8 yr	Moderate	4 yr	Antecubital fossae	7 wk *	None	None	None
M R	11 yr	Severe	2 wk	Face, neck, antecubital and popliteal fossae	5 wk *	100%	More than 75%	None
R G	8 mo	Severe	6 mo	Face, neck, antecubital and popliteal fossae	6 wk *	More than 50%	More than 50%	Insomnia
D F	5 yr	Moderate	7 mo	Neck, antecubital and popliteal fossae	5 wk *	More than 50%	More than 50%	None
K F	18 yr	Mild	17 yr	Face	3 wk *	100%	More than 75%	None
E P	42 yr	Severe	5 mo	Face, neck, antecubital fossae	2 wk *	More than 75%	More than 75%	None
S F	6 mo	Severe	5 mo	Face, neck, wrists, pop liteal and antecubital fossae	4 wk *	More than 75%	More than 50%	Insomnia
D C	22 yr	Severe	4 yr	Face, neck, antecubital and popliteal fossae	3 wk *	100%	More than 75%	None
T E	9 mo	Moderate	2 mo	Face	3 wk *	More than 25%	More than 50%	None
J P	3 yr	Moderate	30 mo	Face, neck, antecubital and popliteal fossae	3 wk †	More than 75%	More than 75%	None
F A	6 mo	Moderate	4 mo	Face	2 wk *	None	None	None
E W	52 yr	Moderate	3 yr	Face	3 wk *	More than 50%	More than 50%	None
E T	24 yr	Severe	20 yr	Face, neck, antecubital and popliteal fossae	2 wk *	None	None	None
S G	7 mo	Moderate	6 mo	Face, antecubital and popliteal fossae, legs	1 wk †	More than 50%	More than 50%	None
A S	48 yr	Severe	2 mo	Face, neck, arms	7 wk *	More than 75%	More than 75%	None
C G	3 yr	Mild	2 yr	Antecubital and popli teal fossae	5 wk *	100%	100%	None
C D	44 yr	Moderate	14 yr	Face, axillas	1 wk *	More than 50%	More than 50%	None
G K	22 yr	Mild	9 yr	Antecubital fossae	3 wk *	More than 75%	More than 75%	None
E A	37 yr	Moderate	6 yr	Antecubital and popli teal fossae	3 wk †	Worse	None	Itching worse after 1 week

Control Patients

Patient	Age	Degree of Eruption	Duration of Eruption	Region Affected (Bilaterally)	Length and Type of Treatment	Results of Treatment in Percentages of Improvement	
						Area Treated with Phenindamine	Control Area
W B	18 mo	Moderate	1 yr	Antecubital and popliteal fossae	3 wk, phenindamine to left side and ointment base to right side	More than 50%	No change
D C	13 yr	Moderate	3 yr	Neck, antecubital fossae	2 wk, phenindamine to left side and ointment base to right side	More than 75%	No chance
J R	52 yr	Severe	18 yr	Neck, arms	1 wk, phenindamine to left side and ointment base to right side	More than 50%	No change
R H	18 mo	Severe	6 mo	Face, neck, ante cubital and popli teal fossae	6 wk phenindamine ointment followed by 1 wk with ointment base	More than 75%	Relapse with ointment base
F B	6 mo	Mild	2 mo	Face	1 wk, ointment base	Cleared	
S D	19 yr	Severe	15 yr	Face, neck, ante cubital and popli teal fossae	2 wk ointment base	No change	
L B	4 mo	Moderate	2 mo	Face, antecubital and popliteal fossae	2 wk, with ointment base followed by 2 wk with phenindamine	No change with ointment base More than 50% improved with phenindamine	

* The asterisk indicates the use of oral and local therapy
† The dagger indicates the use of local therapy alone

that phenindamine is a potent local anesthetic and that it is longer acting, in equivalent concentrations, than procaine

In addition to these effects, phenindamine has some properties which are the opposite of those of the more familiar antihistaminic drugs It minimizes a histamine-induced vasodepression in cats, and it is necessary for one to administer ten to twenty times as much histamine intravenously to secure a fall in blood pressure following the administration of 1 mg per kilogram of phenindamine as would be needed to secure a similar fall without phenindamine Likewise, in man the principal symptomatic effects have been nervousness, sleeplessness and irritability rather than the more familiar hypnotic reactions which are customarily seen when other antihistaminic substances are employed

CLINICAL STUDIES

Technic—In this study we have employed phenindamine in a syrup containing 10 mg per 4 cc, in tablets containing 25 mg each and in a 5 per cent ointment in a carbowax 1500[5] vehicle

Two series of patients were treated The first series was of persons with disseminated neurodermatitis (atopic eczema) and consisted of 23 treated and 7 control patients The second series consisted of persons with circumscribed neurodermatitis (lichen chronicus simplex) and contained 14 treated and 3 control patients In addition to these 1 patient with disseminated neurodermatitis and another with circumscribed neurodermatitis were treated with the compounds Nu-1326 and Nu-1525 The essential data regarding the diseases of the patients treated with phenindamine and of the control patients appear in tables 1 and 2

Of the patients with disseminated neurodermatitis 9 of the treated group and 3 of the control group gave a family history of allergic disease, while no such history could be elicited in the rest With 1 exception the entire group of patients with disseminated neurodermatitis were treated during the winter, and that portion of the study was terminated before warmer weather occurred and before any spontaneous clearing could be noted in other patients not included in this report The exception was a control patient (S D), whose eruption had been present since birth and showed no seasonal variation

Phenindamine was employed in the form of the hydrogen tartrate salt in the tablets and the syrup The phosphate salt was used in the ointment The compound Nu-1326 (2-methyl-9-phenyl-2,3-dihydro-1-pyridindene) was in the form of the hydrobromide salt, while Nu-1525 (2-methyl-9-phenyl-2,3,4,4a-9,9a-hexahydro-1-pyridindene) was used as the amine

The doses employed by us were not as large as those used by Kesten and Sheard[5] Our dose for adults was usually 25 mg, given three times daily, and it was never more than 100 mg daily The total daily dose for infants was 15 to 20 mg, and that for children, 30 to 40 mg

Customarily, the ointment was applied three times daily and was gently massaged into the skin It was applied to acute, weeping areas without hesitation No other treatment was given to the patients during the time that phenindamine phosphate or the ointment base was used All patients showing any signs of

5 Kesten, M B, and Sheard, C Treatment of Allergic and Some Other Dermatoses with Thephorin, J Invest Dermat **9** 65-66 (Aug) 1947

lasted only one week there was no relief of itching and no improvement in the appearance of the lesions

Miscellaneous Dermatoses During the course of this study we treated a small number of patients with diseases other than neurodermatitis Three patients with urticaria received phenindamine tartrate orally, and all 3 experienced complete relief from itching and a reduction in the size and number of the lesions present but not complete disappearance of the lesions Several patients with pruritus vulvae and pruritus ani have been treated also, with good symptomatic relief

Side Reactions—Of the group of patients with disseminated neurodermatitis there were 5 who had reactions to medication Four were infants who received phenindamine orally and locally All 4 became restless and irritable and slept poorly These symptoms subsided completely within twenty-four hours after the drug was discontinued by the oral route but continued locally The fifth patient was the only one of the series who became worse during treatment The itching of this patient became severer one week after the beginning of treatment Patch tests gave negative results

Three of the 14 patients with circumscribed neurodermatitis had relapses while under treatment Since the nature of the relapse was not clear, each patient was given patch tests One of these patients (F M) showed an edematous, erythematous reaction in forty-eight hours after patch testing with the phenindamine phosphate ointment A patch test with the ointment base had negative results

In addition to the patients reported here we have had called to our attention 1 other patient, whose reaction we consider worthy of note This person, a patient of Dr John Seddon, began to have insomnia after two weeks of treatment with phenindamine, 25 mg twice daily Because of the sleeplessness the dosage of phenindamine was reduced to 25 mg in the morning, and the patient was given diphenhydramine hydrochloride, 25 mg at night The insomnia grew still more severe and the patient began to suffer from pain in the thighs and increased sweating She remained mentally clear, but her symptoms progressed, and muscular incoordination and numbness in legs and arms increased so that she could hardly climb stairs and began to drop kitchen utensils There were no accompanying neurologic signs The symptoms completely abated within three days after treatment with phenindamine was discontinued

COMMENTS

The literature is replete with references to the use of antihistaminic drugs in disseminated and circumscribed neurodermatitis With regard to oral administration of the previously used antihistaminic compounds it

clearing of the eruption The skin of those patients has remained clear to date This result is in agreement with observations in other forms of therapy for this disease in that cure occurs so seldom that the clinician is content to have his patients comfortable, to bring them some degree of improvement and to expect no more So far as we could tell, there was

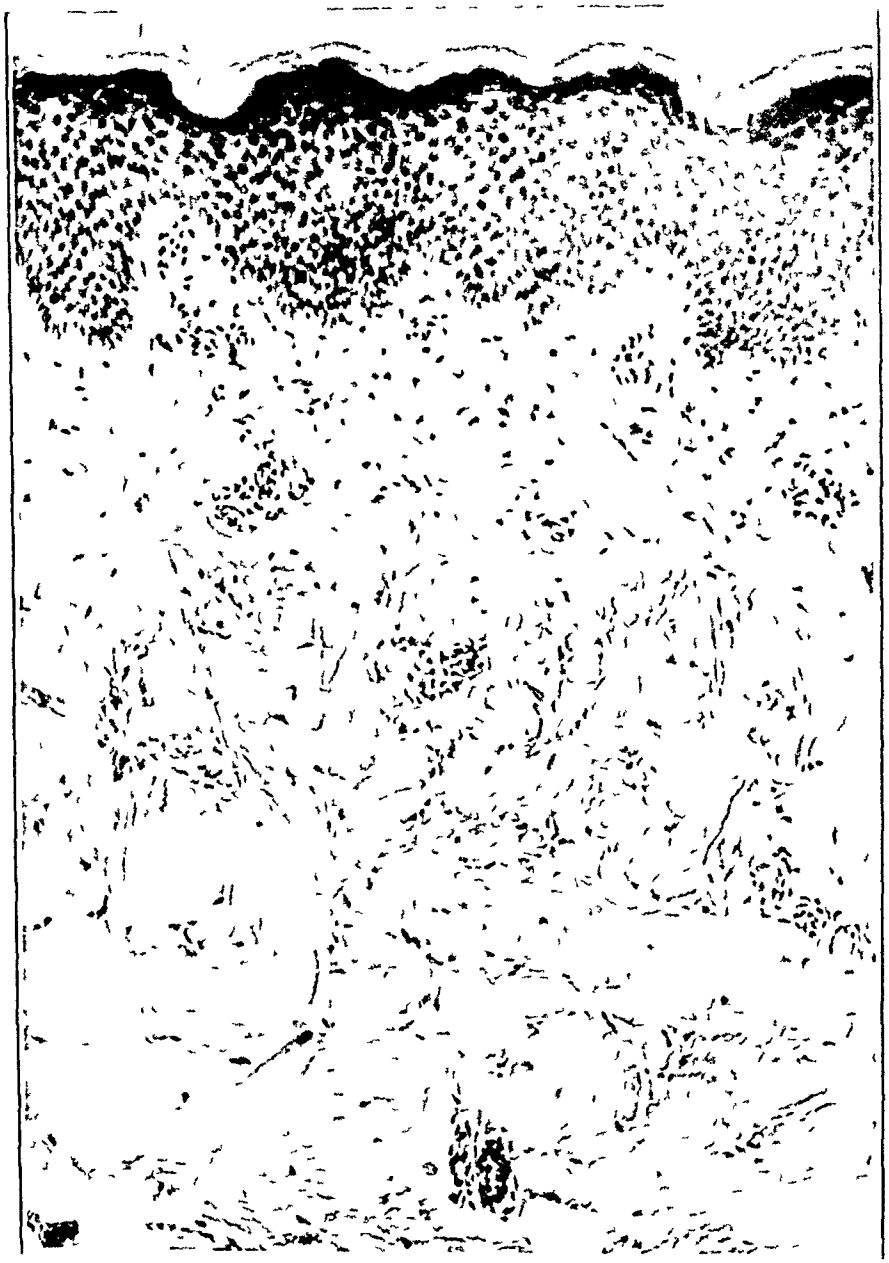


Fig 3—Photomicrograph of skin from an identically involved area of the right antecubital space of patient (D S), after two weeks of treatment with phenindamine (× 115) The progress toward a more nearly normal epidermis and the diminution of the edema, vascular dilatation and round cell infiltration in the cutis are clearly seen

no difference between the response to treatment of the so-called "atopic" group, i e, those with a positive family history, and that of those without

It is well known that both diphenhydramine hydrochloride and tripelennamine hydrochloride are local anesthetics, however, their failure to diminish itching when applied locally would seem to indicate that their penetrability is low, a property which is overcome to some extent by ion transfer Phenindamine, on the other hand, is obviously able to penetrate the skin readily, and this property is apparent from both the almost invariable relief of itching and the speed with which relief occurs One of our patients (B B), who had a severe disseminated neurodermatitis, repeatedly insisted that application of phenindamine phosphate ointment to her antecubital spaces was followed by an almost complete anesthesia lasting for from fifteen to thirty minutes, after which period other sensations returned but itching remained absent for several hours Casual testing of the reaction of this patient to pinprick, during a period of anesthesia, certainly showed that the sensation of pain was much diminished Most patients did not experience this degree of anesthesia Admittedly, however, it is not clear to us how much of the improvement noted in these patients was due to relief of the sensation of itching and how much was due to a genuine healing effect caused by the medication employed It has long been a generally accepted observation that patients with either the disseminated or the localized form of neurodermatitis have had improvement of the condition when their pruritus was relieved Whatever the mechanism which resulted in the relief of the patients in our series, we can say it yielded more satisfactory results than any topical agent heretofore employed

The most frequent reactions to phenindamine tratrate administered orally (sleeplessness and irritability) were not seen when phenindamine phosphate was applied only locally The sedative effects of diphenhydramine hydrochloride and tripelennamine hydrochloride, while being desirable on occasions, are also important as occupational hazards [11], the danger accompanying the use of those drugs is obviated by the local use of phenindamine

CONCLUSIONS

A new antihistaminic drug, phenindamine, is discussed

This drug is chemically unrelated to and pharmacologically distinct in many of its effects from previously employed antihistaminic compounds

The results of the use of phenindamine in the treatment of circumscribed and disseminated neurodermatitis and other itching dermatoses are presented and discussed

11 Slater, B J , and Francis, N Benadryl Contributing Cause of Accident, J A M A **132** 212-213 (Sept 28) 1948 Arnold, H L Benadryl in Chronic Urticarias, Arch Dermat & Syph **54** 71 (July) 1946

If it was to occur definite improvement in the eruption was noted within a week in all cases Once improvement became evident it was progressive but usually reached a peak within four weeks Even though no more improvement occurred in most patients after that time, they could be maintained in an improved condition and were content to continue treatment even though they made no further progress Actual relapse during treatment was noted only rarely

It may be seen from table 1 that 3 of the patients were treated with the ointment alone In addition to these there were 3 patients who received phenindamine tartrate orally together with tars locally before a supply of the phenindamine phosphate ointment arrived From these patients we could conclude with reasonable certainty that phenindamine tartrate administered orally was of little or no benefit in this disease and that the ointment was almost entirely responsible for the improvement seen

Figures 2 and 3 illustrate the degree of histologic clearing which occurred in 1 of the patients of this group (D S) The first photomicrograph was made from a specimen taken for biopsy from the right antecubital space before treatment with phenindamine was begun The second specimen, also from the right antecubital space, was taken after two weeks of treatment from an area which initially had shown identical involvement The patient was an 11 year old girl who had had a constant severe, disseminated neurodermatitis for ten years

The control series of 7 patients were treated in various ways, as noted in table 1 Except in the case of 1 patient who had a mild eruption on the face (F B), treatment with the ointment base was of no benefit, while treatment with phenindamine promptly caused improvement Figure 4 shows the result of one week of treatment in 1 of the control patients (J R) with the ointment base applied to the right forearm and phenindamine phosphate ointment to the left

A patient with disseminated neurodermatitis was treated locally with the compounds Nu-1326 and Nu-1525 One of the compounds was used in the antecubital space on one side and the other in the opposite space After one week a very slight decrease in itching was noticeable in the area treated with Nu-1326, and no change at all was attributable to Nu-1525 After this treatment the patient received phenindamine therapy, with prompt improvement

Circumscribed Neurodermatitis As was stated previously, the results obtained with phenindamine in the treatment of the series of patients with circumscribed neurodermatitis were not as satisfactory as those secured in the other group Data referable to the treatment of patients with circumscribed neurodermatitis are recorded in table 2

Circumscribed neurodermatitis was treated as satisfactorily with phenindamine as with any other topical medication and with the added

STUDIES OF SWEATING

II On the Mechanism of Action of Local Antiperspirants

MARION B SULZBERGER, M D
FREDERICK G ZAK, M D
AND
FRANZ HERRMANN, M D
NEW YORK

ALTERATIONS of sensible perspiration are known to occur under the influence of the autonomic nervous system (e g, stimulation after injection of pilocarpine or acetylcholine and inhibition through the use of atropine through degeneration of peripheral nerves, and by use of local anesthetics) Moreover, the alterations occurring during the course of certain clinical diseases (e g, miliaria rubra [prickly heat] and tropical anhidrotic asthenia) have recently received intensive study [1] But little is known of the mechanism involved in the modifications of sweat secretion which are routinely produced through topical remedies, such as the common topically applied "antiperspirants'

In fact, there is somewhat more information concerning the process of topical stimulation of sensible perspiration In recent clinical, experi-

Read at the Sixty-Eighth Annual Meeting of the American Dermatological Association, Inc, Coronado, Calif, April 28, 1948

From the Skin and Cancer Unit, Department of Dermatology and Syphilology (Dr Marion B Sulzberger, Director), New York Post-Graduate Medical School New York University-Bellevue Medical Center

1 (*a*) Sulzberger, M B, and Emik, L O Studies on Prickly Heat I Clinical and Statistical Findings, J Invest Dermat **7** 53, 1946 (*b*) Sulzberger, M B, and Zimmerman, H M Studies on Prickly Heat II Experimental and Histologic Findings, ibid **7** 61, 1946 (*c*) Sulzberger, M B, Zimmerman, H M, and Emerson, K, Jr Tropical Anidrotic Asthenia (Thermogenic Anhidrosis) and Its Relationship to Prickly Heat, ibid **7** 153, 1946 (*d*) Sulzberger, M B, Herrmann, F, and Zak, F G Studies of Sweating I Preliminary Report with Particular Emphasis on a Sweat Retention Syndrome, ibid **9** 221, 1947 (*e*) O'Brien, J P Miliaria Rubra, Tropical Anhidrosis and Anhidrotic Asthenia, Brit J Dermat **59** 125, 1947 (*f*) Unna, P G Kritisches und historisches uber die Lehre von der Schweissekretion, Schmidt's Jahrb **194** 89, 1882 (*g*) Ueber die insensible Perspiration der Haut, Verhandl d Kong f inn Med, 1890, p 230 (*h*) Wolpert, H Die Wasserdampfabgabe der menschlichen Haut im eingefetteten Zustand, Arch f Hyg **41** 306, 1901-1902 (*i*) Rothman, S Ueber den Einfluss einiger dermatotherapeutischer Grundsubstanzen auf die insensible Wasserabgabe der Haut Arch f Dermat u Syph **131** 549, 1921

advantage that itching became reduced to absent while treatment was continued In this disease, improvement in the appearance of the lesion often was not seen until as long as two weeks after the beginning of treatment, although itching was promptly relieved after application of the ointment In the group with circumscribed neurodermatitis, as opposed to the other, there was a tendency for initial subjective and

TABLE 2—*Data on the Treatment with Phenindamine of Patients with Circumscribed Neurodermatitis*

Patients Treated with Phenindamine *

Patient	Age	Degree of Eruption	Duration of Eruption	Region Affected	Length of Treatment	Results of Treatment in Percentages of Improvement: Subjective	Objective	Reactions
S W	56	Severe	20 yr	Right instep	7 wk	50% initially, relapse under treatment	50% initially, relapse under treatment	Negative reaction to patch tests
M K	58	Moderate	10 yr	Nuchа	3 wk	More than 75%	More than 75%	None
B B	38	Moderate	12 yr	Insteps, elbows, palms	5 wk	100% initially, relapse under treatment	75% initially, relapse under treatment	Negative reaction to patch tests
F M	51	Severe	8 yr	Right ankle	10 wk	25% initially, relapse under treatment	25% initially, relapse under treatment	Positive reaction to patch tests
M H	66	Mild	5 yr	Nuchа	10 wk	100%	Less than 50%	None
M P	36	Moderate	6 yr	Right palm	10 wk	100%	Less than 50%	None
J N	62	Moderate	5 yr	Right thigh	3 wk	100%	More than 50%	None
B H	55	Moderate	8 yr	Nuchа	2 wk	More than 75%	Less than 50%	None
L B	46	Moderate	2 yr	Insteps	3 wk	100%	More than 75%	None
M B	58	Moderate	8 yr	Nuchа, hands	2 wk	More than 75%	More than 50%	None
G T	31	Moderate	2 yr	Scrotum	4 wk	100%	More than 50%	None
K W	38	Severe	12 yr	Nuchа	6 wk	Less than 50%	None	None
E G	66	Moderate	16 yr	Nuchа	3 wk	More than 75%	More than 75%	None
E B	72	Mild	3 yr	Nuchа	2 wk	Less than 50%	None	None

Control Patients

Patient	Age	Degree of Eruption	Duration of Eruption	Region Affected	Length and Type of Treatment	Results of Treatment: Subjective	Objective
J D	48	Moderate	6 yr	Nuchа	2 wk with ointment base	No change	No change
T H	62	Severe	15 yr	Left ankle	2 wk with ointment base	No change	No change
B T	57	Moderate	11 yr	Nuchа	2 wk with ointment base	No change	No change

* Only local medication was given to patients with circumscribed neurodermatitis

objective improvement to be followed by relapse while treatment was continued These patients received ointment alone, and the relief of itching seemed as great for them as for those with disseminated neurodermatitis, most of whom received both oral and local therapy

The 3 control patients with circumscribed neurodermatitis were treated only with the ointment base, and none showed either any improvement in the appearance of the lesions or any relief of itching

One patient with a lesion on each instep was treated with the compounds Nu-1326 and Nu-1525, one to each lesion Although treatment

Three other men used a cream the composition of which is as follows

Formula B

Waxy components glycol stearates and stearic acid	16%
Emulsifying agents solution of sodium alkyl benzene sulfonates (W 102)[2]	4%
Light liquid petrolatum U S P	2%
Hydrated aluminum sulfate	20%
Inert filler	13%
Water	44%

Two other men used both formulas, one in each axilla

Formula A was found by clinical observations and electrohygrometric determinations (by means of a special electrohygrometer [11d]) to be much more effective in reducing sensible perspiration than was formula B

Preparation A was used by an additional subject (female) once daily in "routine fashion" for two consecutive weeks before a biopsy specimen was taken from the axilla Another person (male) used preparation A in a single application on the armpit one hour before a biopsy specimen was taken (after preceding electrohygrometric examinations had shown that the beginning of antiperspirant action was manifest in this case within forty minutes after the application) On 2 control persons the vehicle of preparation A was applied to the axillas in three consecutive applications prior to biopsy, just as on the 8 test persons

All biopsy specimens were cut completely in serial sections, after fixation in Bouin's fluid and embedding in paraffin

RESULTS

None of the subjects exhibited any gross, clinically discernible, alteration, irritation or inflammation at the sites where the antiperspirant creams were applied In several instances, in particular after the use of formula A, antiperspirant activity was distinctly noticeable at the time of the removal of tissue for biopsy A definite reduction of sensible perspiration had occurred in the woman who had used preparation A for two consecutive weeks

HISTOLOGIC OBSERVATIONS

In striking contrast to the absence of any clinical irritation, a considerable inflammatory reaction in the cutis of each specimen was revealed at microscopic examination This reaction was distinctly more pronounced after the application of formula A than after the use of formula B It should be stressed at this point that all the other alterations, such as degenerative changes of the sweat apparatus, to be described later, were likewise definitely less after the application of preparation B than after that of the stronger antiperspirant, A

In the axillas of 2 control subjects who had received applications of the blank vehicle of preparation A, and in the axillas of persons who had received no applications, the characteristic changes were absent

ECCRINE GLANDS

The cellular elements of the inflammatory reaction consisted—in conformity with what might be expected, considering the short duration

has been generally agreed[6] that they are of some value in relieving itching but that they have no other effect on the course of the disease

The use of these drugs in local therapy of neurodermatitis has not been as extensive Perry[7] concluded that diphenhydramine hydrochloride applied in ointment form was of no value in neurodermatitis and of debatable value in other diseases Feinberg and Bernstein[8] found that tripelennamine hydrochloride ointment had a favorable effect in relieving the itching of disseminated neurodermatitis however, their findings could not be confirmed by Sulzberger and his associates[9] One of the few favorable reports on the local use of previous antihistaminic substances in neurodermatitis was that of Sulzberger, Baer and Levin,[9] who employed tripelennamine hydrochloride ointment and reported that half of their 16 patients with circumscribed neurodermatitis showed not only a diminution of itching but also a clinical improvement An additional 25 per cent of their patients showed transitory improvement only a prominent feature of our own series treated with phenindamine

The only other report of local therapy of neurodermatitis with antihistaminic drugs which seemed to be of benefit to the patient was that of Aaron, Peck and Abramson[10] These investigators employed tripelennamine hydrochloride in an aqueous solution and introduced the drug into the skin by iontophoresis They reported 2 cases of circumscribed neurodermatitis and 1 of disseminated neurodermatitis which greatly improved with treatment

6 Friedlander and Feinberg[2] Osborne, E D , Jordon I W and Rausch N G Clinical Use of a New Antihistaminic Compound (Pyribenzamine) in Certain Cutaneous Disorders, Arch Dermat & Syph **55** 309-321 (March) 1947 Logan, G B Histamine Antagonists in the Treatment of Allergic Disease in Children, M Clin North America **31** 948-953 (July) 1947 Baer, R L , and Sulzberger, M B Pyribenzamine in the Treatment of Itching Skin Conditions J Invest Dermat **7** 147-150 (July) 1946 Levin, S I Beta-Dimethylaminoethyl Benzhydryl Ether Hydrochloride (Benadryl) Its Use in Allergic Diseases, J Allergy **17** 145-150 (May) 1946 Friedlander, A S The Use of a Histamine Antagonist, Beta-Dimethylaminoethyl Benzhydryl Ether Hydrochloride in Allergic Disease, Am J M Sc **212** 185-191 (Aug) 1946 Friedlander, A S , and Friedlander, S Pyribenzamine in Hay Fever and Other Allergic Disorders, J Lab & Clin Med **31** 1350-1354 (Dec) 1946

7 Perry, D J The Local Use of Benadryl Ointment, J Invest Dermat **9** 95-97 (Aug) 1947

8 Feinberg, S M , and Bernstein, T B Pyribenzamine Ointment for the Relief of Itching, J A M A **134** 874-875 (July 5) 1947

9 Sulzberger, M B , Baer, R L , and Levin, H B Local Therapy with Pyribenzamine Hydrochloride, J Invest Dermat **10** 41-42 (Feb) 1948

10 Aaron, T H , Peck, S M , and Abramson, H A Iontophoresis of Pyribenzamine Hydrochloride in Pruritic Dermatoses, J Invest Dermat **10** 85-90 (Feb) 1948

From the foregoing statements it is clear that at a somewhat later stage enough inflammatory cells will have worked their way through the epithelial barrier to appear in large numbers in the lumens of the



Fig 2—Two eccrine ducts after application of antiperspirant A (low power view) They are inflamed, and the one on the left is greatly dilated

sweat ducts Whether their presence in this location acts as a barrier to the outflow of sweat is a matter of conjecture

There was no evidence of narrowing of sweat pores

It is believed that the use of this drug represents a significant advance in the treatment of neurodermatitis, as improvement can be obtained with local therapy alone This form of treatment has been entirely free from constitutional reactions, and we have encountered only 1 case of induced sensitivity In our hands, phenindamine ointment seems to be the best drug available for the treatment of disseminated neurodermatitis In the treatment of circumscribed neurodermatitis, though beneficial in most cases, it was not as effective as in that of the disseminated disease

Cherry and Kimbrough Streets
Washington and Theresa Avenues (3)

APOCRINE GLANDS

In the apocrine glands, as in the eccrine pores, there was nowhere any evidence of a narrowing of the ostiums of the ducts In other respects, however, the observations for the apocrine glands, which—as



Fig 4.—Apocrine gland after application of antiperspirant A, showing the expulsion of nucleoli from the nuclei (oil immersion lens)

is well known—open into hair follicles above the level of the sebaceous glands, were of an entirely different nature

One of the earliest changes observed in otherwise normal-appearing apocrine glands was expulsion of the nucleolus into the cytoplasm of the cells of the acini This was followed soon by dissolution of the nucleus (caryolysis) or by its pyknosis If the damage to the lining

mental and histologic studies, O'Brien [1c] elucidated the increased excretion of eccrine sweat through local application of wool fat Similar observations had been made by P G Unna [1f,g] and later by Wolpert [1h] and by Rothman [11], and we could confirm O'Brien's observations in our own investigations The provocatory action of the hydrophilic fats on sensible perspiration is, according to O'Brien, intimately related to the degree of patency of the sweat pores, the size being increased or maintained in the presence of these fats on the surface of the skin

The reverse of this process, namely narrowing of the openings of the sweat ducts, is generally regarded as the cause of decreased or inhibited sweating under the influence of the widely used antiperspirant preparations Pharmacologists and dermatologists quite uniformly ascribe this effect to the astringent properties of the active ingredients, this ascription applying equally whether the preparation contains aluminum salts, zinc salts, formaldehyde or resorcinol Occasionally also the adsorbent action of the metal salts in use is mentioned as an effective mechanism

It was our hope that histologic examinations might shed some light on the mechanism of action of these topical antiperspirants, especially on the more or less hypothetic and experimentally unproved conception of a merely dehydrating and astringent action. It is the object of this report to give some very preliminary information on histologic observations of the skin of grossly normal axillas of healthy persons after the application of several commonly employed antiperspirant creams

METHOD

The exact history of each person being tested was taken with special reference to the intensity of sensible perspiration and the previous use of antiperspirants for example A considerable interval had to precede the test applications of the antiperspirant in those instances in which an antiperspirant preparation had been used previously For each application an amount of the preparation of approximately the volume of a pea was used, gently rubbed in with the finger tips as is customary On 8 men three applications to each axilla tested were made at twelve hour intervals before the biopsy specimen was taken No washing was allowed in the interim in these cases, but taking of a specimen for biopsy was always immediately preceded by removal of the remnants of the cream with water and by careful, soapless shaving On 3 of these men an antiperspirant cream of the following formula was applied

Formula A

Waxy components glycol stearates and stearic acid	12%
Emulsifying agents solution of sodium alkyl benzene sulfonates (W 102)[2]	8%
Hydrated aluminum sulfate	20%
Inert filler	13%
Water	47%

2 W-102 is produced by Wallace Laboratories, Inc, 53 Park Place New York

This process frequently involved one gland and spared the one immediately adjacent

The cast material, which might well act as a mechanical obstacle to the outpouring of sweat, not rarely appeared to have been carried with the sweat stream, so to speak, and eventually lodged in the



Fig 6—Apocrine glands after application of antiperspirant A (high power dry lens) The acini on the left show numerous cellular casts in their lumens, while the group on the right appears normal

perpendicular portion of the apocrine duct From the foregoing observations it is clear that, in contrast to what was observed in the eccrine glands, the main changes in the apocrine glands occurred in the secretory tubule Changes in the duct were secondary

of the application primarily in polymorphonuclear leukocytes with varying admixtures of lymphocytes These cells appeared to be attracted to the area of the uppermost portion of the eccrine sweat ducts,



Fig 1—Eccrine pore after application of antiperspirant preparation A, showing acute inflammation of duct and neighboring vessels (high power dry lens)

perhaps by the positive chemotaxis of the material or its derivatives that had entered through the sweat pore As these cells were of hematic origin, it goes without saying that the vessels of the upper corium frequently were the site of perivascular inflammation

degeneration does not become apparent in every apocrine gland, the proportion of visibly damaged glandular elements is considerable

Not only the alteration of the epithelium but also the desquamation of these lining cells into the lumens of the ducts might have a bearing on the impaired delivery of sweat on the surface It is conceivable that this castoff material acts as a plug in the ducts Furthermore, the possibility cannot be denied that the concentration of inflammatory elements around an eccrine duct may produce a stenosing, flow-obstructing ring

From these considerations it is evident that additional investigations are needed to clarify further the mechanism of antiperspirant action At present it appears possible, or even probable, that several interdependent or independent factors contribute to the effect

The conspicuous infiltrative inflammation around and through the epithelium of the eccrine ducts, and even into their lumens, and likewise the almost selective degeneration of elements of the apocrine glands are highly suggestive of a special chemotaxis of the active antiperspirant ingredients It is possible that aluminum soaps are formed by interaction of the applied aluminum sulfate and some of the fatty acids along the ducts and that this process brings about the described changes An interesting and also most unexpected clinical observation is not inconsistent with the aforementioned assumption After the application of the antiperspirant preparation and before demonstrable decrease of sensible perspiration, one can observe an individually variable period during which there is actually a provocatory effect on the excretion of sweat Similar to the effect obtained after application (and removal) of wool fat,[1e] increased production of sweat can be demonstrated with the starch-iodine test in this early phase following application of the antiperspirant formula

We shall not here describe in detail the occasional clinical inflammatory reactions we have observed after the use of antiperspirants in general However, it may be noteworthy that such reactions are observed chiefly or only in persons with strong axillary perspiration, who feel the need of using antiperspirants We also find it noteworthy that we have repeatedly seen these relatively rare reactions occurring in several members of a family, e g , in mother and son, and in a father and his two daughters More observations are needed to decide whether or not this familial occurrence is only coincidental

SUMMARY

Twelve biopsy specimens were taken from the axillary skin of healthy volunteers after application of two antiperspirant preparations containing aluminum sulfate as the active ingredient All the specimens were cut serially There were distinct reactive alterations in the cutis

It should be emphasized at this point that in the majority of biopsies the changes just discussed were not seen in all eccrine ducts but in a sizable percentage, which varied from case to case It is interesting to note that the changes in the eccrine glands were confined to the

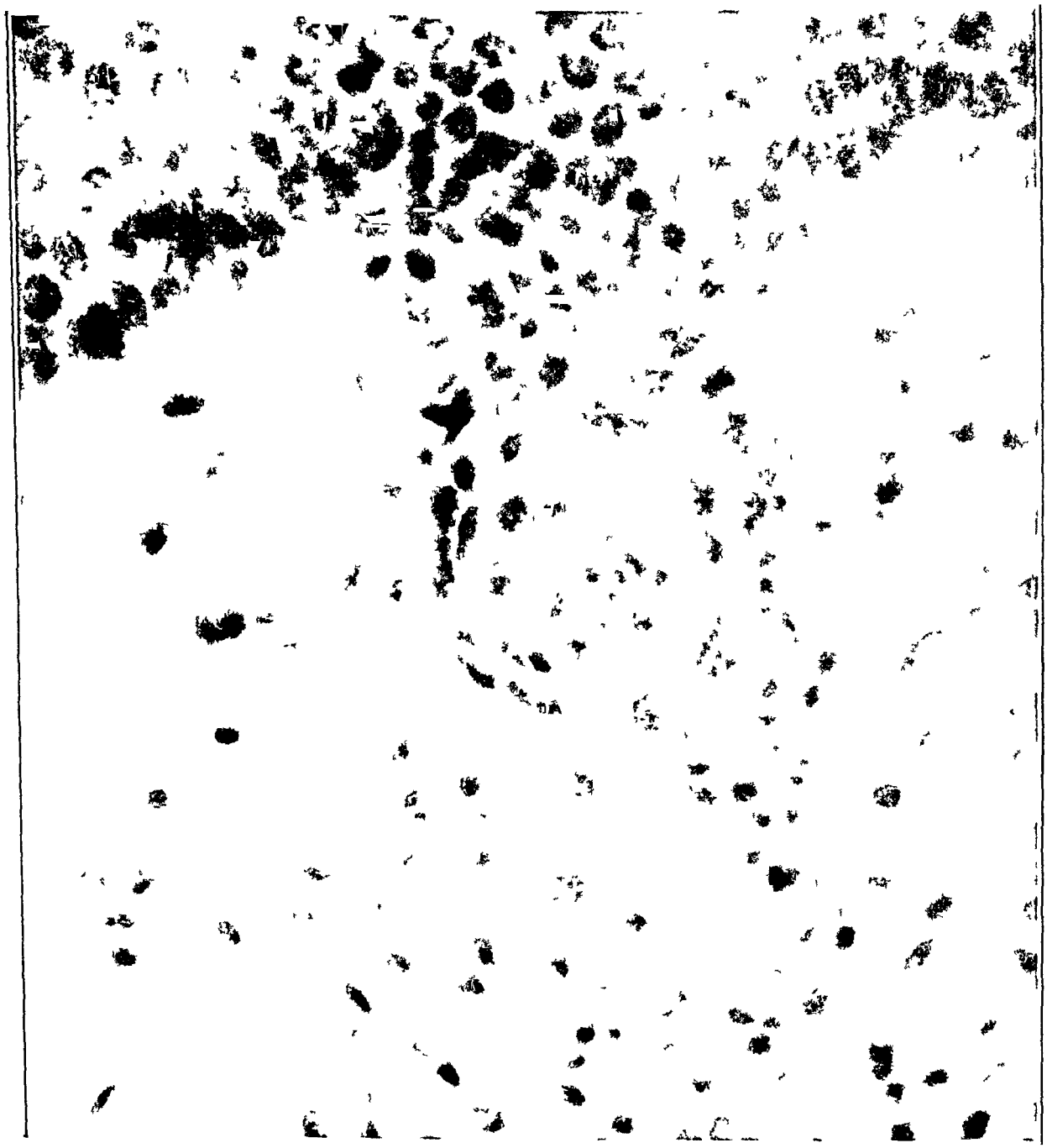


Fig 3—Eccrine duct after application of antiperspirant A, showing inflammatory cells which have penetrated into the lumen (high power dry lens)

straight portion of the ducts In 5 biopsies (4 persons) an occasional eccrine gland and duct was seen to have appreciable diffuse dilatation The significance of this observation is not clear as yet

It is interesting to note that there is a decided clinical difference between the effectiveness of formula A and that of formula B Chemically the difference between these two formulas is that formula B contains 2 per cent more light petrolatum and an increased amount of waxy substances With this small increase in the amount of light petrolatum, the aluminum sulfate was not effective and little or no antiperspirant effect was noted

The degeneration of the apocrine glands might well account for the fact that these antiperspirants also have a deodorant effect, because most of the odor of the axilla and the pubic area is due to these glands

This investigation is fundamental and of extreme importance for a better understanding of disturbances in sweating

Dr Samuel M Peck, New York Dr Sulzberger deserves a great deal of credit for undertaking this work Time and again, those of us who have had to discuss the action of antiperspirants before various government agencies have had to rely on theoretic explanations for the actions of these materials This is the first time that I have had the pleasure of having presented to me factual material concerning the action of the antiperspirants on the skin and an explanation of what actually occurs when perspiration is diminished I should like to have Dr Sulzberger explain to me the mechanism by which abscesses are formed after the use of antiperspirants After hearing the paper and seeing the histologic changes, I conclude that perhaps it would be better for one to use a deodorant instead of an antiperspirant to eliminate body odors

Dr Herman Sharlit, New York Frankly, I was somewhat shocked to see these observations at the clinic I watched these experiments, and I can assure you that every procedure was used to make this report correct I want to present a point of view with respect to the meaning of these data which should be taken into consideration It is properly what might be anticipated, that the application of a new, concentrated metallic salt to the skin would do a certain amount of damage in some way This report gives the evidence of the damage Certain physiologic factors show that there was apparently a slowing up of the rate of sweat production That slowing up is not necessarily due to the pathologic changes evidenced here It is known that this slowing up is maintained Therefore, it would be necessary to demonstrate that by continual use of this material one would continue to give evidence of this type of infiltration mechanically produced It might be that the person becomes inured to this irritant and that the reaction would not persist Dermatitis, pustulation and papulation occur, and use of the preparations must usually be given up Commercial manufacturers do not by any means distribute most of the antiperspirants Women give a prescription of their own, in which aluminum chloride is used, to their druggists As for the matter of deodorizing, I don't think that these compounds do any good One simply masks one odor with a stronger one

Dr. John Belisario, Sydney, Australia I should like to start by asking Dr Sulzberger if he would tell what the actual vehicle was that was employed When I discussed miliaria rubra with O'Brien, who performed and wrote the first work on this subject in connection with tropical anhidrosis and hyperkeratosis of the mouths of the sweat glands, he informed me that the wool fat employed did not stimulate sweating but rather made the keratin permeable, so that the sweat dammed back could permeate to the surface I believe this explanation to be correct

I very much appreciated the paper, it is really a fine piece of work and should help a great deal in the elucidation of this subject This paper is in keeping with

cells was severe enough they disintegrated, leaving a denuded membrane behind [2a]

Desquamated lining cells, apparently washed away by the secretory pressure, appeared as cellular casts in various portions of the gland



Fig 5—Apocrine gland, after application of antiperspirant A (high power dry lens) The section of the tubule at the bottom evidences disintegration of epithelium, while the section at the top contains cellular casts

2a The lining of the aprocrine gland is much more likely to show regressive changes and detachment from its basement membrane than is that of the eccrine gland, a fact which makes postmortem study of normal control material unsatisfactory

previously used to produce local outpouring of sweat, it probably acts by clearing the pore openings and by hygroscopic action on the sweat in the ducts

It must be obvious to all physicians why we at the Skin and Cancer Unit and Department of Dermatology and Syphilology of the New York University-Bellevue Medical Center have been and continue to be so interested in the mechanisms and pathologic changes of sweating Sweating and aberrations of sweating are of profound importance both in dermatology and in many other branches of medicine What my co-workers and I have recently labeled "the sweat retention syndrome" can lead to pricking and itching and scratching, to vesicle formation (dyshidrosis, miliaria) and to inflammation, when the sweat which should normally be poured out on the skin's surface is blocked and remains within the tissues and either forms pools and vesicles around the sweat glands or trickles through into the surrounding tissues When the quality of sweat being absorbed is great, there can be toxic manifestations, local lymph node enlargement and perhaps other local and general effects Moreover, the failure of the normal mechanism of cooling by the outpouring and evaporation of sweat can lead to a variety of general medical disturbances which may have profound temporary or lasting effects on the respiratory, cardiovascular and nervous systems All the symptoms of this syndrome are likely to be most pronounced when non-secretory evaporation of fluid is not sufficient to cool and when secretory sweating is called on continuously or repeatedly, as is the case in workers and worriers in constantly hot and humid environments I believe that one of the main reasons why so many patients with a variety of cutaneous eruptions—for example, atopic dermatitis, various eczematous and eczematoid eruptions, dyshidrosis and certain fungous infections (not to speak of asthma, sinusitis and arthritis and other nondermatologic diseases)—so often do well in a dry, even-temperatured environment and when freed from "tensions" may well be that under these last-mentioned conditions these persons do not so often require sweat secretion in order to cool and to lose fluid and are therefore largely freed from the sweat retention syndrome

One more suggestion in closing—many drugs, foods and other absorbed agents and metabolites normally may be wholly or partially excreted in secreted sweat When the pore is blocked, all these are not excreted but retained in—one might even say "injected into"—the tissues I should like you to think about the possible consequences of these literally millions of intracutaneous injections per day (adult man has an estimated 2,000,000 sweat pores) in relation to allergic sensitization and desensitization phenomena and to allergic diseases, for example, allergic eruptions due to drugs such as quinacrine or the eczematoid eruptions which sometimes exacerbate on exposure to foods or inhalants, e g, atopic dermatitis and perhaps other eczematoid dermatoses of the hands

I thank you all again for your attention and encouragement, and I hope that my collaborators, Dr Franz Herrmann and Dr Frederick Zak, and others of my department will soon have more to report on this subject of aberrations of sweating

An occasional mitotic figure was seen in an apocrine duct, while mitosis of apocrine gland cells was missing This absence of regeneration is to be expected to be seen in short term experiments like ours

All the alterations, inflammatory and degenerative, described in the foregoing paragraphs were observed very early indeed and were already present to the full degree in the biopsy specimen taken one hour after a single application of formula A

COMMENTS

Perhaps the least expected, but at the same time the most distinct and uniform, observation in these histologic studies is the invariably present inflammatory reaction

For practical reasons it may be pointed out that the presence of this microscopically observed inflammation does not indicate that antiperspirant preparations are more harmful than they are generally considered to be For millions of people are using these products effectively and without suffering any harm On the other hand, the generally known occasional appearance of clinical inflammatory reactions under the influence of antiperspirants is readily understood in the light of our observations

The other unexpected, though clear, result of our histologic investigations is the discovery that the usual assumption of an astringent action of antiperspirants, with consequent narrowing or collapse of the openings of the sweat ducts, finds no support whatsoever in our microscopic studies With our technic it was seen that most, if not all, of the ostiums were wide open after use of the preparations

Although our present histologic observations give no single, simple explanation of the mode of action of the antiperspirants used in these experiments, it appears probable that the described inflammatory reaction and degenerative alteration of the sweat glands are involved in the mechanism of the decrease of sensible perspiration This assumption is in agreement with the fact that a weaker inflammatory response was observed microscopically after application of the less effective antiperspirant preparation, B, than was seen after use of the more effective formula, A and the absence of the characteristic changes in the control specimens

One of the most conspicuous changes which may explain diminished sweat excretion in the axillas is the described degenerative alteration of the apocrine glands Because of this there are certainly less cells available for sweat production The fact that the degenerative process is manifest in the apocrine coils rather than the eccrine glands, where the inflammatory process prevails, is readily understood when one considers the much greater frailty of the apocrine glands While the

Cases of Erythroplasia of Queyrat as Reported in the American Literature

Authors	Race, Sex and Age	Total Duration of Lesions	Evidence of Malignant Degeneration	Evidence of Circumcision	Evidence of Syphilis	Treatment and Results
Sulzberger and Satenstein [a] (Presented by Lapowski * 2 yr later and by Lapowski and Walzer [5] 6 yr later)	W M 39	9¾ yr	None	No mention	None	Filtered and unfiltered roentgen rays, no improvement electrocoagulation, recurrence in 3 to 4 mo
Smith and Hughes [4a]	Mexican M 24	1½ yr	None	Yes	None	Electrocoagulation and solid carbon dioxide, small area of recurrence after 9 mo
Irgang and Alexander [4l]	Negro M 77	5½ yr	None		None	Electrocoagulation, no recurrence after 14 mo
Hall Hoffman and Newman [4c]	W M 61	2 yr	Squamous cell	No	Yes	Amputation of penis and removal of inguinal lymph nodes
Stiles [4d]	W M 42	Unknown	None	No	Yes	Electrocoagulation, no follow up
Schwartz [4e]	W M 31	4 mo	None		None	〃
Tauber [4f]	Negro M 38	6 yr	None	No	None	〃
Throne [4g] (Presented by Lapowski * 5 mo later and by Lapowski and Walzer [5] 5 yr later)	Jew M 49	6¼ yr	None	〃	None	Electrocoagulation on two occasions, recurrence
Fox [4h]	W M 25	10 mo	None		〃	〃
Schiller [4i]	W M 36	3 wk	No biopsy	No	Yes	〃
Rosenthal [4j]	W M 62	6 to 7 yr	Basal cell carcinoma	No	None	〃
MacKee [4k]	W M 70	10 to 15 yr	Yes		None	Bland local therapy, progressive roentgen irradiation amount unknown, no benefit
Friedman [4l]	W M 38	1½ yr	No biopsy	〃	None	?
Callaway [4m]	W M 24	1 yr	None		〃	Bismuth intramuscularly and filtered roentgen rays, no benefit
Schmidt [4n]	W M 69	2½ yr	Yes	No	None	Filtered roentgen rays, no benefit
Rosen [4o]	W M 24	3 yr	None		None	?
Combes [4p]	W M 39	2 yr	Yes	No	None	Bismuth intramuscularly and bland local therapy no benefit
Freeman and Engler [4q]	W M 62	7 yr	None	No	None	Filtered roentgen rays, no benefit
LaRocco [4r]	W M 53	2½ yr	None	?	None	Antisyphilitic therapy no benefit

* Lapowski, B Erythroplasia of Queyrat, Arch Dermat & Syph 33 160 (Jan) 1936

These changes were much more pronounced after the application of the more effective of the two preparations and were absent in the control specimens The essential histologic observations were as follows

In the eccrine sweat glands there was considerable cellular infiltration through the epithelium of the perpendicular portion of the ducts, together with perivascular cuffing in the upper corium (polymorphonuclear leukocytes and lymphocytes)

In many of the apocrine sweat glands there were degenerative alterations of the lining of a great part of the acini (tubules), with conspicuous desquamation of epithelial cells and formation of cellular casts

There was no narrowing or collapse of the ostiums of the ducts of either eccrine or apocrine glands

Possible implications of these data for an explanation of the mode of action of antiperspirants are discussed, and the need for further investigations is emphasized

999 Fifth Avenue

25 East Ninety-Fourth Street

962 Park Avenue

ABSTRACT OF DISCUSSION

DR FREDERICK G NOVY JR, Oakland, Calif Dr Sulzberger and his co-workers are to be congratulated on continuing their valuable investigations on the disturbances of sweating in various diseases

In the past there had been no truly investigative work done on antiperspirants It had been assumed that the action of antiperspirants is an astringent one, causing narrowing of the sweat ducts or actual temporary stenosis of the sweat ducts so that less perspiration reaches the skin and thus there is a reduction of sweating Today, Dr Sulzberger has clearly shown from his histologic studies that this is not the case He has demonstrated that with the eccrine glands there is an inflammatory infiltrate about the duct This inflammation tends to narrow the duct orifice so that less perspiration is produced The glands themselves are not affected

In the case of the apocrine glands there is a degeneration of the secretory cells, which in turn causes a decreased production of their fluid This degeneration of the cells of the apocrine gland occurs rapidly after death, so that some of the changes could be explained on the basis of the death of cells On the other hand, Dr Sulzberger has clearly shown in his histologic observations that there are cellular casts along with the degeneration, which combination tends to produce plugging of these glands

These findings are quite different from those of Dr Sulzberger and his coworkers in prickly heat, thermogenic anhidrosis and the sweat retention syndrome In these three conditions decreased production of sweat was due to actual plugging of the duct orifices by keratinized material and hyperkeratosis surrounding the duct opening Again, in cases of postquinacrine dermatitis, Dr Sulzberger found that a different condition prevailed to cause the decrease in sweating In the latter condition, the failure to sweat existed because of actual atrophy and destruction of the sweat ducts due to the severe inflammation caused by the quinacrine dermatitis

of cells of the epidermis Some portions showed spotty hyperkeratosis and parakeratosis In some regions there were definite wildness and disturbances of cells, with intraepidermal squamous cell malignant change Other rete plugs showed portions of irregular mitosis with numerous dyskeratotic cells In the dermis there was an extensive lymphocytic and plasma cell infiltrate, in many portions the infiltrate extended into the rete plug and produced miliary abscesses There was pronounced edema, with separation of the collagen fibers No tumor masses were seen in the dermis

The cause of this entity is unknown Certain predisposing conditions are recognized, chief among these is an inherited predisposition to develop cutaneous malignant changes, e g, a rough, dry skin Chronic irritation is undoubtedly a factor, Lapowski and Walzer[5] were cognizant of this fact and employed protection from irritation by a metal tubular shield in treating 2 cases In the

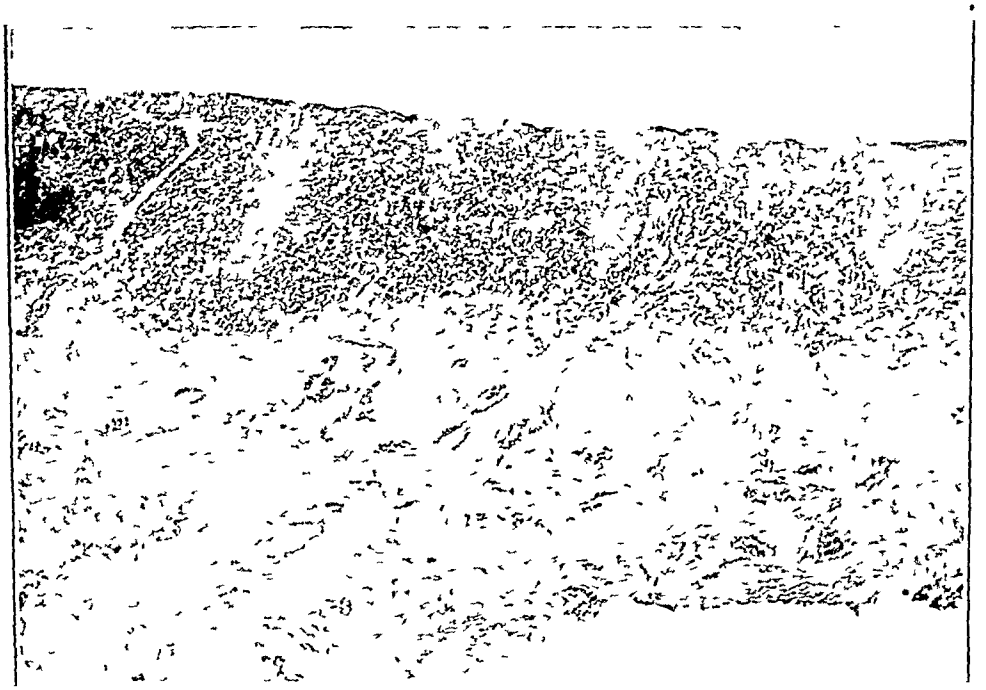


Fig 2—The irregular acanthosis, elongated and broadened papillae and the pronounced edema and vascular dilatation in the corium should be noted The intense cellular infiltrate is sharply demarcated below (Hematoxylin and eosin stain × 40)

European literature syphilis has often been mentioned as an etiologic factor Cases reported in the American literature have not borne this out, however, in only 3 of the cases was there evidence of syphilis, in our case there were no indications of the disease The question of uncircumcision in etiology seems to have been largely neglected by previous authors, reports of 9 of the 19 cases containing no information on this point There was 1 case in which circumcision had been performed, and another in which it seemed likely that it had, the patient being a Jew In 8 of the cases the patient was uncircumcised

5 Lapowski, B, and Walzer, A Erythroplasia of Queyrat, Arch Dermat & Syph **39** 184 (Jan) 1939

all of Dr Sulzberger's work on the subject, which has been outstanding and is admired by us in Australia

DR MARION B SULZBERGER, New York I thank Dr Novy and the rest of you for your kind and pertinent discussions

Like Dr Novy, we too were astonished by the radical changes in effects produced by what seems to be but a minor change—not in the "active ingredient," but only in the vehicle employed But that result is in entire accord with what I have seen in relation to the effects of vehicles of many topical agents, including such diverse agents as various local medicaments, insect repellents, protective films and ointments against poison gases or agents used on the skin or in wounds for bactericidal or fungicidal effects A slight alteration in the vehicle chosen can make a tremendous difference in the effects achieved

I am particularly happy to hear Dr Peck's remarks If, as we suspect, the changes seen under the microscope in our studies are actually pictures of the principal mechanism through which the antiperspirant effects of these agents are brought about, then in the future the biopsy and the microscopic pictures may provide one of the objective ways of studying the effectiveness of antiperspirants of this type

As far as Dr Peck's question regarding the sweat gland abscesses or rather, the apocrine gland abscesses, is concerned, no such abscesses were produced in any of our 10 test subjects However, it is well known that, as Dr Peck states, the clinical use of antiperspirants is sometimes (fortunately most rarely) followed by sweat gland abscesses in the users The mechanism of the formation of such abscesses may perhaps be explained by the pictures we found It is noteworthy that, as a result of our interest in these problems, we found in our great clinical material in which antiperspirants were used only 5 cases of sweat gland abscesses and it is most remarkable that these 5 cases all occurred in two families, 2 in one family (mother and son) and 3 in another family (father and two daughters) Of course these figures are insufficient to permit one to draw conclusions, but it seems to me conceivable that the tendency to sweat gland abscesses may be in a measure dependent on local anatomic or functional anomalies of the sweat glands and that these anomalies can well be hereditary and thus of familial occurrence

In reply to Dr Sharlit's generous remarks, all we can now say is that the changes we have described are the only ones we saw which could account for the reduction of sweating after the local use of these antiperspirants There are still great gaps in our knowledge here, and our studies are being continued All we now know about the time intervals concerned is that the changes observed can appear as early as sixty minutes after one application of the antiperspirant and that in the few cases studied thus far the changes had disappeared on histologic examination two weeks after the last application of an antiperspirant Moreover it seems that the same changes can occur in persons who use antiperspirants habitually as took place in those volunteers who in the course of our present studies used them for the first time

I thank Dr Belisario for his kind words With the exception of the light petrolatum added in formula B, all the ingredients in both formulas were the same —such as the same wetting agent and the same fillers—but the proportions of "fats' and wetting agent were somewhat different I shall be glad to give Dr Belisario further details if he wishes them and to tell him where he can obtain the exact specifications

What Dr Belisario said about Dr O'Brien's fine work and the action of wool fat is absolutely correct Wool fat does act differently from many agents

glans penis and foreskin All cases reported in the American literature have been in men Other reported sites of involvement are the scrotum, the vulva, the buccal mucosa, including the tongue and the lips, the cheek, and the back

The differential diagnoses include Bowen's disease, Paget's disease (carcinoma simplex of nipple), leukoplakia, kraurosis, lupus vulgaris (tuberculosis luposa), eruption due to drugs, psoriasis, eczema, syphilid and lichen planus Darier pointed out that in cases clinically identical, dyskeratotic changes which are definitely of the type of Bowen's disease have been found If the conception of Civatte is accepted, erythroplasia is nothing more than Bowen's disease of the mucous membranes Clinically, crusting is regularly present in Bowen's disease but not necessarily in erythroplasia, histologically, Ash [7] stated the belief that there is more fibrosis present in erythroplasia than is seen in either leukoplakia or Bowen's disease

Extramammary cases of Paget's disease occur (this observation has been disputed by some persons), Busman and Woodburne [8] reported a case involving the glans penis The histologic picture of Paget's disease is typical, however The absence of apple jelly nodules should serve to exclude tuberculosis luposa An eruption due to drugs, a patch of psoriasis of eczema or of lichen planus or a syphilid can usually be ruled in or out by appropriate procedures Distinctive exudative discoid and lichenoid dermatosis of Sulzberger and Garbe caused confusion in 1 instance Early there is localization of this condition to the penis and the tip of the nose, later, generalized lesions appear

The treatment of erythroplasia has been a subject for much discussion among previous authors No form of treatment seems to be universally successful, radiation therapy has proved unsatisfactory, cryotherapy has been followed by recurrences Endocrine therapy has not been reported The best treatment short of radical operation appears to be complete removal, with a safe margin, by electrocoagulation

In 5 of the 19 cases there was histologic evidence of malignant degeneration, of basal cell carcinoma in 1 instance and of the squamous cell variety in the other 4 In 1 of these cases there was regional glandular enlargement In 12 of the cases there was no histologic evidence of malignant changes, however, usually only one biopsy specimen was taken In 2 cases there were no biopsies The duration of the disease in the first-mentioned group ranged from two years to twelve and one-half years, or an average of five and one-tenth years, in the group showing no evidence of malignant degeneration the range was from four months to nine and three-fourths years, or an average of approximately three and nine-tenths years In this regard, in our case there was histologic evidence of early squamous cell degeneration with the lesion having been present but three months There was no regional adenopathy, however

SUMMARY

A case of erythroplasia of Queyrat with carcinoma in situ is presented and previously reported cases reviewed The recommendation by Ash that "malignant dyskeratosis" replace "precancerosis" in terminology is advocated

3241 Burnet Avenue

7 Ash, J E Personal communication to the authors

8 Busman, G J, and Woodburne, A R Paget's Disease of the Glans Penis, with Central Carcinomatous Degeneration, Arch Dermat & Syph **24** 396 (Sept) 1931

Clinical Notes

MALIGNANT DYSKERATOSIS, ERYTHROPLASIA OF QUEYRAT TYPE

Report of a Case

WILLIAM E McDANIEL, M D
AND
LESTER M MASON, M D
CINCINNATI

Erythroplasia is a malignant dyskeratosis of unknown etiology, first described in 1893 by Fournier and Darier,[1] who designated it as epithelíome papillaire The name erythroplasia was suggested in 1911 by Queyrat,[2] who described in detail several cases of what appeared to be an identical condition Sulzberger and Satenstein[3] reported the first case in the American literature in 1933, we have found accounts of 18 additional cases, for the most part in society transactions (table) [4] This report adds 1 more case to the slowly growing number

From the Department of Dermatology and Syphilology, the University of Cincinnati College of Medicine, and the Cincinnati General Hospital

1 Fournier, A, and Darier, J Épithelíome bénin syphiloide de la verge (epithelíome papillaire), Bull Soc franç de dermat et syph **4** 324, 1893

2 Queyrat Érythroplasie du gland, Bull Soc franç de dermat et syph **22** 378 (Nov 9) 1911

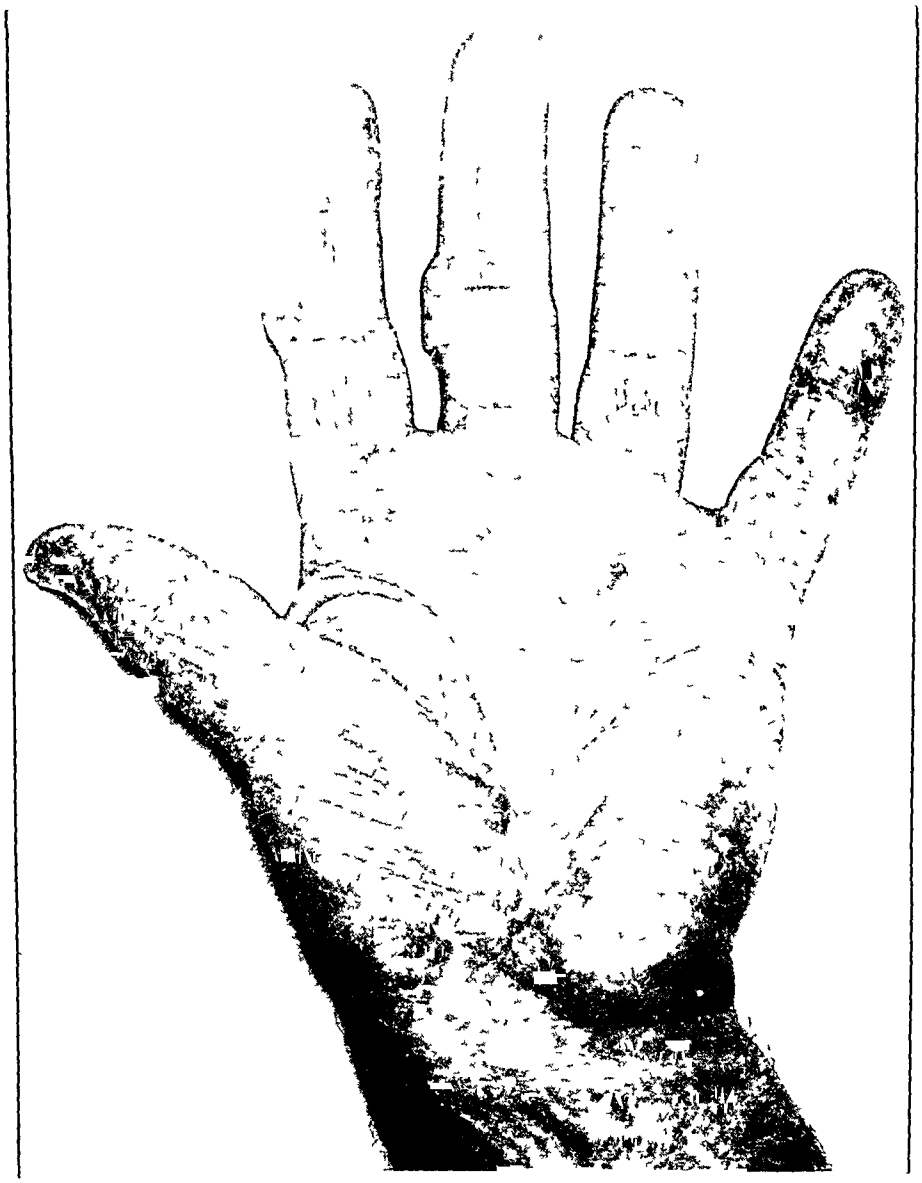
3 Sulzberger, M B, and Satenstein, D L Erythroplasia of Queyrat, Arch Dermat & Syph **27** 798 (Dec) 1933

4 (*a*) Smith, L M, and Hughes, R D Erythroplasia of Queyrat, South M J **32** 731 (July) 1939 (*b*) Irgang, S, and Alexander, E R Erythroplasia of Queyrat in a Negro, Arch Dermat & Syph **34** 247 (Aug) 1936 (*c*) Hall, T B, Hoffman, R L, and Newman, R Erythroplasia of Queyrat and Carcinoma of Glans Penis Report of Case, Urol & Cutan Rev **39** 21 (Jan) 1935 (*d*) Stiles, F Erythroplasia of the Glans Penis, Arch Dermat & Syph **30** 647 (Nov) 1934 (*e*) Schwartz, H J A Case for Diagnosis (Erythroplasia of Queyrat?), ibid. **30** 594 (Oct) 1934 (*f*) Erythroplasia of Queyrat? case presented by Dr E B Tauber and other members of the Department of Dermatology of the University of Cincinnati College of Medicine and the Cincinnati General Hospital, ibid **34** 160 (July) 1936 (*g*) Throne, B A Case for Diagnosis (Erythroplasia of Queyrat?) ibid **29** 633 (April) 1934 (*h*) Fox, H Erythroplasia, ibid **32** 357 (Aug) 1935 (*i*) Schiller, A E A Case for Diagnosis, ibid **36** 929 (Oct) 1937 (*j*) Rosenthal, T Erythroplasia of Queyrat, ibid **35** 1176 (June) 1937 (*k*) MacKee, G M A Case for Diagnosis (Erythroplasia?) ibid **46** 592 (Oct) 1942 (*l*) Friedman, R A Case for Diagnosis (Erythroplasia of Queyrat?), ibid **41** 1192 (June) 1940 (*m*) Callaway, J Erythroplasia of Queyrat, ibid **42** 350 (Aug) 1940 (*n*) Schmidt, O E Erythroplasia of the Penis, ibid **42** 673 (Oct) 1940 (*o*) Rosen, I Erythroplasia of Queyrat, ibid **42** 981 (Nov) 1940 (*p*) Combes, F C A Case for Diagnosis (Erythroplasia of Queyrat?), ibid **38** 802 (Nov) 1938 (*q*) Freeman, H E, and Engler, J E A Case for Diagnosis (Kraurosis Penis? Erythroplasia of Queyrat?) ibid **43** 206 (Jan) 1941 (*r*) La Rocco Erythroplasia of Queyrat, ibid **40** 456 (Sept) 1939

SYPHILITIC JUXTA-ARTICULAR NODES

FREDERICK KALZ, M D
MONTREAL, CANADA

Recently, I had the opportunity of observing a patient with juxta-articular nodes The unusual localization of these nodules warrants a short report



Multiple nodes on the fingers and palms of left hand

REPORT OF A CASE

A 54 year old white Canadian, unaware of his syphilitic infection, had observed during the previous four years slowly growing painless nodes on the fingers and palms of both hands One node was removed surgically, and the diagnosis

From the Section of Dermatology, Sub-Department of Medicine, Dr J C Meakins, Physician in Chief, Royal Victoria Hospital

REPORT OF CASE

History—T R, an unmarried white man aged 71, was first seen in the dermatologic clinic of the Cincinnati General Hospital on Jan 10, 1947, he was referred from the genitourinary clinic (where he was being treated for multiple urethral strictures) because of a persistent erythematous patch on the dorsum of the glans penis The lesion was of three months' duration and asymptomatic, it had been first noticed as an erythematous spot, centrally located on the dorsum of the glans penis, in October 1946 At that time the lesion had been the size of a small pea and nonelevated, it gradually enlarged peripherally, but the patient was little concerned because of a lack of symptoms

Nothing pertinent was elicited from the family or personal past history The patient has been retired on a pension for fifteen years Prior to his retirement he had worked for thirty years as a street cleaner and street repairer, and for eighteen years as a carriage driver There was no history of syphilis diabetes or ingestion of drugs



Fig 1—The sharp margination of the lesion and the dry, erythematous surface may be seen The scar near the corona is at the site of removal of tissue for biopsy

Examination—A sharply demarcated, irregularly rectangular, erythematous patch measuring 25 mm by 19 mm involved the dorsum of the glans penis and the corona, the lesion was a plaque, elevated about 1 mm The involved area was of slightly greater firmness than the surrounding tissue and had a velvety appearance, the surface was completely dry, and the epithelium was intact No enlarged lymph nodes were found in the inguinal regions The lesion was nontender The skin in general was dry and showed poor turgor, no lesions of the mucous membranes of the mouth were found

A specimen for biopsy was taken by electrosurgery from the proximal margin of the lesion, and the bleeding base was electrocoagulated, the lesion has recurred in the scar made in the taking of tissue No biopsy was made of the lymph glands

The histopathologic report by Dr Leon Goldman was as follows The section showed irregular acanthosis with appreciable differences in the staining quality

extent than with arsenic, penicillin produces a true Herxheimer reaction and suggested that it occurs in 60 per cent of the patients treated This reaction tends to manifest itself as a febrile one rather than as a mucocutaneous flare-up

In early syphilis the Herxheimer reaction is of little consequence, but in patients with late syphilis, in which the syphilitic activity may be located in vital structures, the Herxheimer reaction is potentially dangerous [2] Likewise, this potential danger may exist for the debilitated syphilitic infant

Olansky [3] reported 6 cases in which Herxheimer reactions followed the first injection of as little as 1,000 units of sodium penicillin I have seen rapid deterioration in 2 cases of dementia paralytica, and Callaway and associates [4] reported exacerbation of psychoses within the first few days of treatment with penicillin There are reported cases of disastrous outcome in the treatment of cardiovascular syphilis with penicillin by Moore,[1] Dolkart and Schwemlein [5] and Callaway [4] However, that the Herxheimer reaction was the cause of fatal outcome was not definitely established in these cases

Notwithstanding the suggestion by some authors that the Herxheimer reaction may be beneficial in that it simulates therapeutic inflammation, we at this center feel that prevention of this reaction in some cases of infantile congenital syphilis and late syphilis would be advantageous

Consequently, a study was undertaken in which the use of a strong antihistaminic substance was employed in an effort to abort the Herxheimer reaction Diphenhydramine hydrochloride (beta-dimethylaminoethylbenzohydryl ether hydrochloride [benadryl hydrochloride®]) was used Curtis and Owens,[6] Shaffer and associates,[7] Friedlaender [8] and others have demonstrated its influence in urticaria, which may be due to liberation of histamine into the tissues More recently, Friedlaender suggested that the action of diphenhydramine hydrochloride is one of competing with histamine at the receptor organ rather than one of chemical neutralization of histamine

A series of 247 consecutive patients with previously untreated primary and secondary syphilis were placed on an antisyphilitic program of 3,000,000 units of penicillin injection in oil and wax U S P, five arsenical treatments and three bismuth treatments in a period of ten days, penicillin alone being given on the first day of treatment In this group we observed an incidence of the Herx-

2 Stokes, J H, and others Penicillin in Late Syphilis Interim Report, Am J Syph, Gonor & Ven Dis **29** 313, 1945

3 Olansky, S The Herxheimer Reactions of Relatively Small Doses of Penicillin, J Ven Dis Inform **28** 26, 1947

4 Callaway, J L, Noojin, R O, Kuhn, B H, Riley K A, and Segerson, J A The Use of Penicillin in Treatment of Syphilis of Central Nervous System, Am J Syph, Gonor & Ven Dis **30** 110, 1946

5 Dolkart, R E, and Schwemlein, G X The Treatment of Cardiovascular Syphilis with Penicillin, J A M A **129** 515 (Oct 13) 1945

6 Curtis, A C, and Owens, B B Beta-Dimethylaminoethyl Benzhydryl Ether Hydrochloride (Benadryl) in Treatment of Urticaria, Arch Dermat & Syph **52** 239 (Oct) 1945

7 Shaffer, L W, Carrick, L, and Zackheim, H S Use of Benadryl for Urticaria and Related Dermatoses A Preliminary Report, Arch Dermat & Syph **52** 243 (Oct) 1945

8 Friedlaender, A S Use of Histamine Antagonist, Beta-Dimethylaminethyl Benzhydryl Ether Hydrochloride in Allergic Disease, Am J M Sc **212** 185, 1946

Schreck and Lenowitz [6] studied a clinical group of 139 men with carcinoma of the penis and compared them with a control group of patients with carcinoma elsewhere They attributed the differences in incidence to variations in sex hygiene

The differential diagnosis of erythroplasia of Quevrat may at times be difficult The lesions are well defined, infiltrated areas with shiny, red, velvety surfaces which may be moist or dry, slightly elevated or flat The commonest site is the

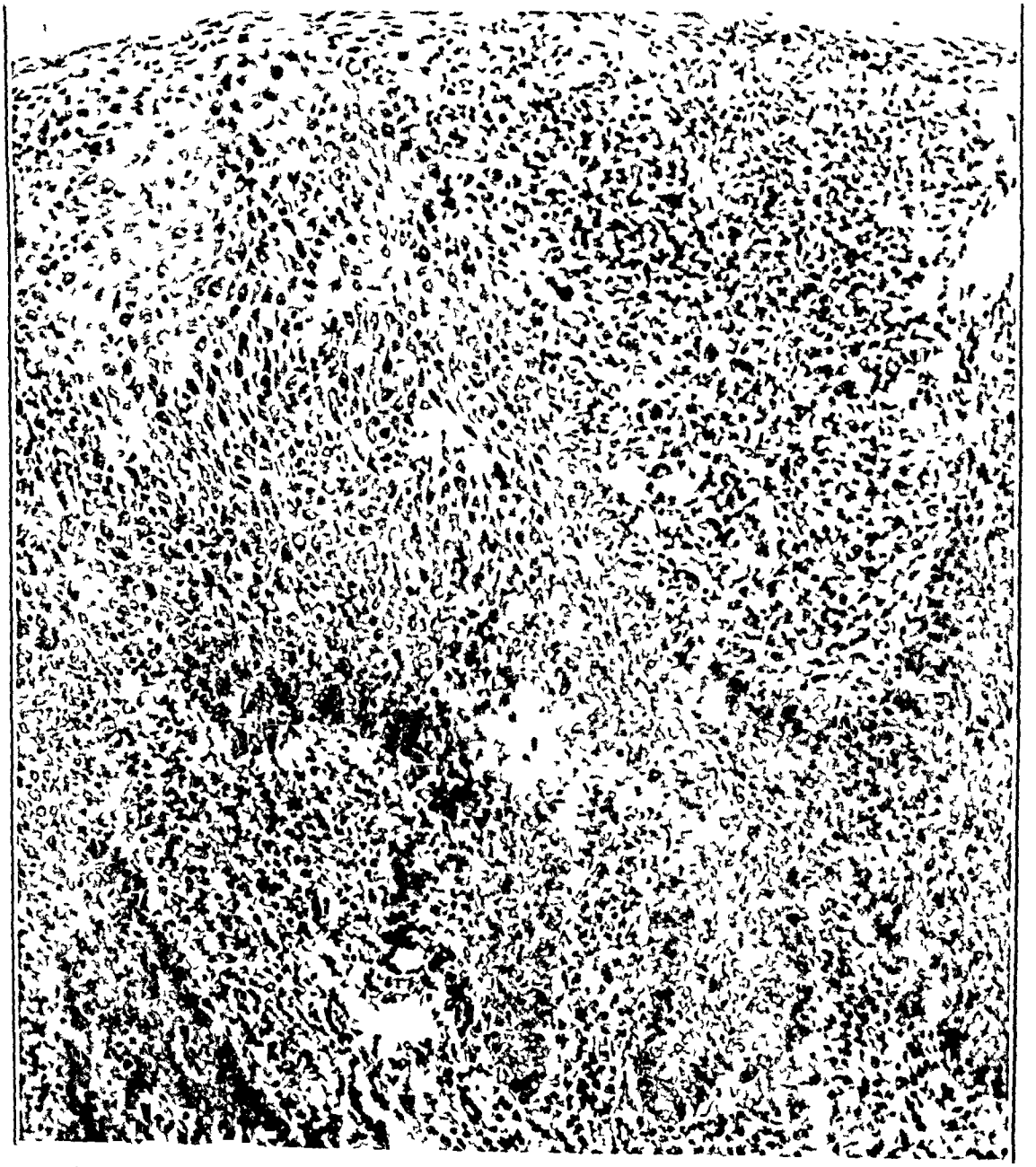


Fig 3—There is appreciable irregular downgrowth of the rete pegs and differences in the staining quality of cells of the epidermis (Hematoxylin and eosin stain, × 160)

6 Schreck, R, and Lenowitz, H Etiological Factors in Patients with Carcinoma of the Penis and in Control Groups, Am J Path **22** 637 (May) 1946

SQUAMOUS CELL EPITHELIOMA AND PSORIASIS

P W HANNAY, M B, Ch B
EDINBURGH, SCOTLAND

Instances of epithelioma arising on areas of skin affected by psoriasis are unusual, and for this reason the following case is reported

REPORT OF A CASE

History—A man aged 45, an engineer, acquired psoriasis in 1922 The disease has been active ever since except for three months' remission in 1930 during a trip to Canada In 1938 the patient discovered that arsenic medication controlled the eruption, and he had been taking solution of potassium arsenite U S P (liquor arsenicalis B P), 3 to 10 minims (0 19 to 0 62 cc) three times daily, with only an occasional discontinuance of the drug for a month at a time The patient's daughter also suffers from psoriasis

In 1942 the patient noted that his palms and soles were becoming "crusted and thickened," that his skin was becoming darker and that an ulcer was developing on a large patch of psoriasis situated on the lower left quadrant of the abdomen The ulcer slowly enlarged and was diagnosed as a squamous cell epithelioma in 1943 The tumor was removed by surgical excision on May 25, and, as there was an enlarged inguinal node on the left side, high voltage roentgen therapy was given Biopsy of the tumor confirmed the clinical diagnosis of squamous cell epithelioma

The patient was first seen at the skin department of the Royal Infirmary, Edinburgh, on June 7, 1946, because of an ulcer which had been present for ten months on the left sacral region

Examination—General physical examination revealed nothing abnormal apart from the following dermatologic condition There were large, scaly, leathery patches of psoriasis over the patient's trunk and limbs, there was profuse scaling of the scalp, and the finger nails showed typical psoriatic pitting The palms and soles showed a pronounced diffuse hyperkeratosis The whole of the trunk, the limbs, the neck and the face were deeply pigmented in a "raindrop" pattern Pigmentation, atrophy and telangiectases were present over both inguinal regions as a result of the previous roentgen treatment given to that area

Situated over the sacral region was a large isolated patch of psoriasis of leathery texture To the left of the midline in the upper gluteal region, and well within the borders of the psoriatic patch, was an ulcerated fungating tumor measuring 4 cm in diameter, it was freely movable over the deeper tissues There was no enlargement of the inguinal nodes (fig 1) Reactions to the Wassermann and the Kahn tests were negative

Report of Biopsy—The section showed two types of lesions (fig 2) To the right of the section there was a squamous cell epithelioma with an ulcerated surface, the tumor, which was in genetic relationship with the epidermis, invaded deeply and penetrated beyond the limits of the biopsy specimen In some areas there was well marked cell nest formation, while in others the cells were less well differentiated Mitoses were moderately numerous There was

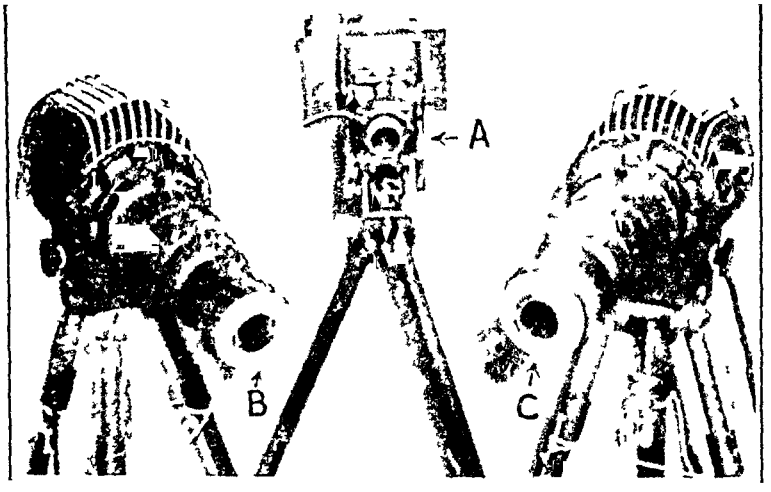
From the Department of Dermatology, the University of Edinburgh Faculty of Medicine

USE OF POLARIZED LIGHT IN COLOR PHOTOGRAPHY OF MUCOUS MEMBRANES

HOLLIS F GARRARD, M D *
MIAMI BEACH, FLA

Polarized light has been used for a number of years in commercial photography to eliminate glare, but, to my knowledge, after a careful search through the available literature, it has not been used for photography of lesions of the mouth Since distracting high lights are often observed in photographs of lesions of the mouth, it was thought that a method to use polarized light would be useful

A method was employed in which polaroid® filters were placed in the light source and over the camera lens The filters were rotated until all glare had



Apparatus for the use of polarized light in color photography of mucous membranes Polaroid® filters are indicated by *A*, *B* and *C*

been eliminated from the image on the ground glass screen This procedure, however, greatly reduced the total amount of light that reached the film Since color film has a slow emulsion speed, it was found that a brilliant source of light was needed in order for the necessity for prolonged exposure to be overcome This problem was met by the use of two 1,000 watt photoflood bulbs in spotlights of condensing type, as illustrated in the accompanying figure The lights are placed 6 inches (15 cm) from the mouth With the setup described, the exposure is 1/25 second at *f* 8, type A kodachrome® film being used, for an image of half the object size If a smaller image with greater depth of field is desired, either a shorter exposure or a smaller diaphragm opening can be used

541 Lincoln Road

* Formerly from the Department of Dermatology, Northwestern University Medical School, Edward A Oliver, chairman



Fig 3—Higher power view of the epitheliomatous area, showing cell nest formation (× 70)

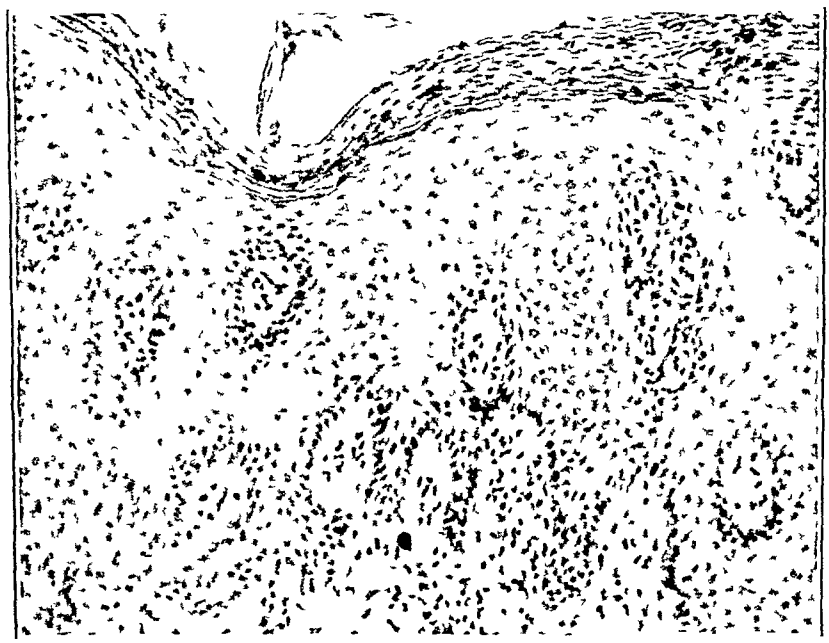


Fig 4—Higher power view of the psoriatic portion (× 100)

of a simple fibroma was made The patient was then referred to me, and examination revealed the following conditions

There were numerous hard, indolent nodes on the palms of both hands and on the palmar and lateral surfaces of the fingers, about the joints They varied in size from that of a split pea to button-like infiltrations about 1 cm in diameter (figure) The overlying skin was normal in color and texture and was easily movable, while the nodules were fixed to the underlying structures There were altogether seven major nodes, five of which were on the left hand In addition, there were a number of smaller nodules, more palpable than visible, and all in the vicinity of articulations Another node was found near the left elbow There were no signs or symptoms of activity of the syphilitic infection The cardiovascular system was normal on both clinical and roentgenologic study, and the neurologic examination revealed no abnormalities The reaction to the Wassermann test of the blood was positive in a dilution of 1 196, and the reaction to the Kahn test was positive The patient had to leave town and was referred to his physician with the diagnosis of late syphilis

We obtained permission to reexamine the previous biopsy specimens and submitted the slides to Dr P H Hartz, pathologist in chief of the Netherlands Public Health Services in Curaçao, who has had the opportunity of seeing and examining many such cases, who happened to be in Montreal at the time He reported observations as follows

"The main feature is the presence of thick bundles of collagen, with occasional lymphocytes, and of areas of cellular infiltration containing large fibrocytes, histiocytes and lymphocytes, forming occasional loose mantles of perivascular infiltration However, there were dense perivascular infiltrations in the border region between the nodules and the surrounding loose connective tissue, consisting of lymphocytes and plasma cells

"In a fibroma with collagenous bundles of comparable thickness, one would expect a more uniform appearance and absence of inflammatory changes The presence of areas of such thick bundles of collagen together with zones of cellular infiltration is characteristic of many of these juxta-articular nodes The absence of intimal thickening makes it difficult to establish histologically the diagnosis of syphilis, but it is known that intimal thickening is by no means a regular finding in these nodes"

SUMMARY

Multiple juxta-articular nodes on the fingers and palms of a white Canadian are described The histologic changes in this case are characteristic of the condition, showing thick collagenous bundles with alternating zones of cellular infiltration

1414 Drummond Street

EFFECT OF DIPHENHYDRAMINE HYDROCHLORIDE (BENADRYL®) ON HERXHEIMER REACTION AFTER USE OF PENICILLIN

JOHN J STEWART, M D
Assistant Surgeon (R), United States Public Health Service
DETROIT

It is an established fact that, in the treatment of syphilis, penicillin causes Jarisch-Herxheimer reactions Moore[1] stated that, perhaps to an even greater

This investigation was carried out at the Detroit Intensive Treatment Center, Herman Kiefer Hospital, Loren W Shaffer, M D, Director

1 Moore, J E Penicillin in Syphilis, Springfield, Ill, Charles C Thomas, Publisher, 1946, p 55

The remaining cases reported[6] were all of basal cell epithelioma arising on psoriatic patches, and in every case the psoriasis had been present for years Some of the patients gave a history of having taken arsenic preparations and some did not

Wright and Friedman's paper[7] on psoriasis and its relation to multiple superficial epithelioma covered the subject fully, despite the fact that in none of the cases presented in it were the two types of lesion superimposed These authors also stated that arsenical epithelioma which develops in persons with psoriasis almost invariably arises independently of any patch of that disease, a view which was also expressed by Ormsby and Montgomery[8]

Details concerning the histochemical technic for determining arsenic in normal and in tumor tissue may be found in the papers published by Osborne[9] and Osterberg,[10] while the histopathologic aspect of arsenical epithelioma was fully discussed by Montgomery in two papers[11], the discussion following one of them[11a] also contained useful comments and inferences concerning Osborne's method for determining arsenic *in situ*

T C Dodds prepared the illustrations

22 Nile Grove (10)

6 Hutchinson, J Arch Surg, London **9** 223, 1898 Hartzell, M B Am J M Sc **118** 265, 1899 Whitfield, A Brit J Dermat **18** 40, 1906 Sequeira, J H Diseases of the Skin, ed 4, New York, The Macmillan Company, 1927, p 558, ibid, ed 5, 1947, p 680 (reference to Gray's case[1]) Flint, E R, and Gordon, J Brit J Surg **16** 321, 1928

7 Wright, C S, and Friedman, R J Psoriasis and Multiple Superficial Epithelioma, Arch Dermat & Syph **27** 70 (Jan) 1933 Franks, A C, and Barner, J S Basal Cell Epithelioma in a Psoriatic Patch, ibid **55** 375 (March) 1947

8 Ormsby, O S, and Montgomery, H Diseases of the Skin, ed 6, Philadelphia, Lea & Febiger, 1943, pp 284 and 746

9 Osborne, E D Microchemical Studies of Arsenic in Arsenical Pigmentation and Keratoses, Arch Dermat & Syph **12** 773 (Dec) 1925, in discussion on Montgomery[11b]

10 Osterberg, A E J Biol Chem **76** 19, 1928 Flint, E R, and Gordon, J Brit J Surg **16** 321, 1928

11 (a) Montgomery, H, and Waisman, M J Invest Dermat **4** 365, 1941 (*b*) Montgomery, H Arsenic as an Etiologic Agent in Certain Types of Epithelioma, Arch Dermat & Syph **32** 218 (Aug) 1935

heimer reaction, as evidenced by a febrile reaction, within the first twelve hours after the initial injection of 300,000 units of penicillin in oil and wax (oxophenarsine hydrochloride U S P [mapharsen®] having been instituted on the second day), of 31 1 per cent (77 patients)

After treatment of the aforementioned group, we placed the next 40 consecutive patients with previously untreated primary and secondary syphilis under the same regimen but gave 100 mg of diphenhydramine hydrochloride orally with the initial injection of 300,000 units of penicillin in oil and wax and 50 mg

TABLE 1—*Frequency of Herxheimer Reactions*

	Number of Patients				Number of Herxheimer Reactions			
	Total Number of Patients	Primary Syphilis		Secondary Syphilis		Total Number	Primary Syphilis		Secondary Syphilis	
		Male	Female	Male	Female		Male	Female	Male	Female
Without Diphenhydramine Hydrochloride	217	93		124		77	34		43	
		74	19	73	51		29	5	19	24
With Diphenhydramine Hydrochloride	40	14		26		19	5		14	
		12	2	10	16		5	0	3	11

TABLE 2—*Percentage Incidence of Herxheimer Reactions*

	Without Diphenhydramine Hydrochloride	With Diphenhydramine Hydrochloride
Incidence of Herxheimer reaction	31 1	17 5
Male patients	32 6	36 3
Female patients	29 0	61 1
Patients with primary syphilis	36 5	35 7
Patients with secondary syphilis	27 9	53 8

of diphenhydramine hydrochloride every four hours thereafter for a total of four doses The incidence of the Herxheimer reaction, as evidenced by a febrile reaction, was found to be 47 5 per cent (19 patients, or nearly half) The detailed analysis of these cases may be seen in tables 1 and 2

Conclusion—As a result of this experience, we feel that diphenhydramine hydrochloride (benadryl hydrochloride®) has no effect in preventing or alleviating the Herxheimer reaction in early syphilis when penicillin injection in oil and wax is used

name Achorion having originally been assigned to a limited number of species of fungi which produced cups [1]

Weidman has pointed out that parafavus, as contrasted with true favus, is accompanied with scutula in small numbers, these usually being confined to one region of the body, such as the lid, scrotum, ear or back, and that residual scarring and alopecia do not always occur Practically all species of Achorion have been incriminated as causative agents of parafavus at various times It is most unusual, however, for other species of fungi, such as the microspora and trichophyta, to incite such an eruption With pseudofavus, cups do not occur, although the instigating fungus is an achorion and potentially capable of inducing the formation of scutula [1]

REPORT OF A CASE

E K., a 24 year old white man, was first seen by us on Oct 14, 1947, complaining of a moderately pruritic scrotal eruption of two weeks' duration The patient's work was such that he came in close contact with milk cattle throughout each day

Physical examination showed normal conditions except for the cutaneous eruption On both the anterior and the posterior aspect of the scrotum were numerous cream-colored scutula of rather uniform size, most being approximately 0 5 cm in diameter (figure) There was an associated pungent, favus-like odor

Microscopic examination of several of the scutula demonstrated them to be composed exclusively of filaments and spores Several culture tubes were inoculated, with a pure growth of Microsporum gypseum (M fulvum) resulting on each within a few days Two weeks of topical therapy with an undecylenic acid compound resulted in complete disappearance of the eruption

SUMMARY

A case of parafavus caused by Microsporum gypseum and restricted to the scrotum is described

1 Weidman, F D, in Blumer, G The Practitioners Library of Medicine and Surgery, New York, Appleton-Century Company, Inc, 1936, vol 10, p 140



Fig 1—Fungating tumor in the center of a psoriatic patch The "raindrop" pigmentation of the surrounding skin is faintly visible

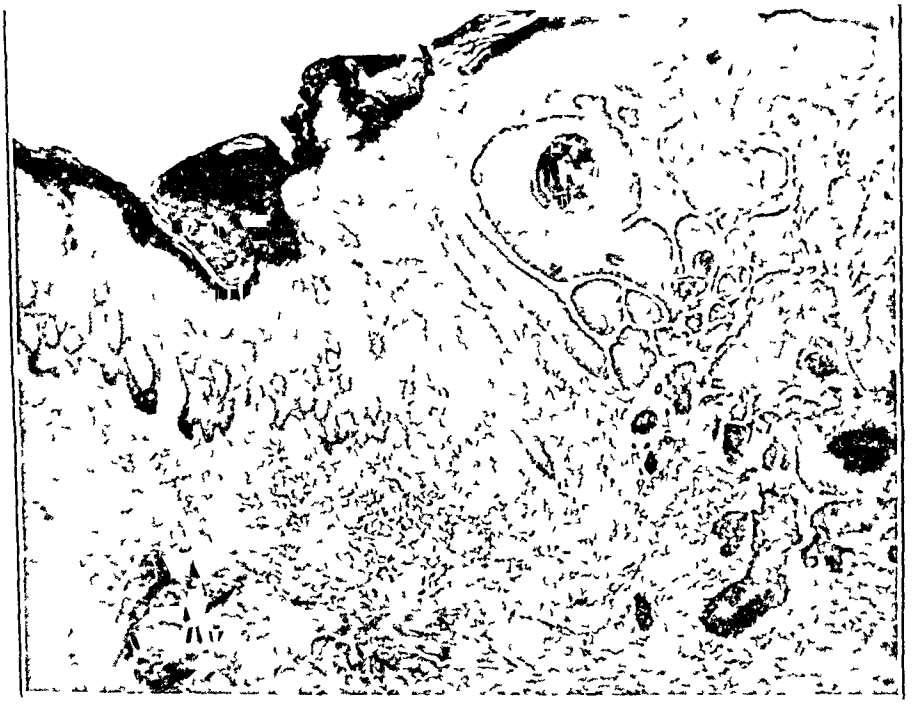


Fig 2—Junction area between the tumors, on the right, and the psoriatic patch on the left (× 25)

Obituaries

PHYLLIS SCHUYLER KERR, M D

1895–1949

Our friend and colleague, Dr Phyllis Schuyler Kerr of White Plains, N Y, died on April 12, 1949, after a long illness Dr Kerr was born in New Brighton, Staten Island, N Y Her father was Walter Craig Kerr, president at the time of his death of Westinghouse, Church, Kerr and Company

Before Dr Kerr entered Rush Medical College of Chicago in 1924 she had been associated with Miss Caroline Pratt as a teacher at the City and Country School of New York city, enjoying the richness of experience with the early workers in progressive education of children Dr Kerr graduated from Rush Medical College in 1928 and served her internship at the State of Wisconsin General Hospital in Madison

From 1929 to 1940 Dr Kerr was associated with the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hosptial From 1930 to 1935 she was office assistant to Dr Fred Wise and Dr Marion B Sulzberger She had been a practicing dermatologist in White Plains since 1936 At the time of her death Dr Kerr was Attending Dermatologist at the White Plains Hospital, Lawrence Hospital of Bronxville, N Y, Tarrytown Hospital, Tarrytown, N Y, and the Westchester Division of the New York Hospital, White Plains She was the chief of the Women's Syphilis Clinic of the Westchester County Department of Health and a member of the White Plains City Planning Board

Dr Kerr was certified by the American Board of Dermatology and Syphilology in 1939 and was a member of the Society of Investigative Dermatology and the Society of Medicine of Westchester County

She is survived by her husband, Max K Sellers, fiction writer, her mother, Mrs Lucy L Kerr, and her sister, Miss Eleanor Kerr, both of New Brighton, another sister, Mrs Vaughan Baker, of Woodbine, N J, and a brother, Donald C Kerr, of Cornell University, Ithaca, N Y

The enthusiasm and kindness which Dr Kerr brought to her work made her a true physician, bringing courage and hope to the suffering and giving inspiration to all those associated with her Her personality was sparkling and warm Always modest and gentle, she carried herself with a quiet and unassuming dignity One of her most endearing qualities was her love for people, and she gave generously of her time and effort to help those with personal, as well as medical, problems Her courage and love of life were contagious and communicated themselves to those associated with her to such an extent that their lives, too, were enriched Her death is a great loss, not only to the medical profession but also to humanity

SAMUEL B FRANK, M D
MARION B SULZBERGER, M D

surprisingly little secondary inflammatory reaction in the surrounding tissue in view of the clinical features of the lesion (fig 3)

To the left of the section the adjoining non-neoplastic skin showed the features of psoriasis (fig 4) Unfortunately, the sections were cut on the slant and so did not accentuate the elongation and ballooning of the papillae, the tips of which approached the surface closely The papillary vessels were dilated, as were those of the subpapillary region, there was a diffuse cellular infiltration, consisting mainly of lymphocytes in the subpapillary layer, and a few cells penetrated the epidermis The epidermis was acanthotic, the stratum granulosum was thinned or absent throughout, and there was decided parakeratosis

Treatment—The tumor was removed by surgical excision on July 17 The psoriasis responded to treatment with salicylic acid (3 per cent) and ammoniated mercury (3 per cent) in petrolatum, followed by application of paste of crude coal tar and, finally, crude coal tar The hyperkeratoses responded satisfactorily to dressings of equal parts plaster of lead oleate N F and petrolatum The patient was discharged as well on September 10, with strict instructions never again to use arsenic He was later seen on Jan 22 and on March 20, 1947, the psoriasis had returned but was controlled with a tar paste (1 per cent), the area of excision showed no neoplastic recurrence, and there was no enlargement of the regional lymph nodes On the second visit it was noted that the palmar hyperkeratoses were becoming troublesome, and treatment with lead compounds and petrolatum was again prescribed

SUMMARY OF THE LITERATURE

A large proportion of the cases of epithelioma which have been reported as arising on psoriatic patches have been of the basal cell variety, and many of the patients had been using arsenic compounds over long periods Gray's case[1] was an example in point A basal cell epithelioma arose on a chronic patch of psoriasis situated in the gluteal cleft of a patient who had been using arsenic preparations for years and yet showed no other signs of reaction to the drug

The case reported by Fordyce[2] was stated to be of a rodent ulcer, but no histologic report was given As the patient subsequently died of metastases in the mediastinal nodes and internal organs, it is probable that the tumor was either squamous or basisquamous in type White's report[3] is interesting mainly for the excellent summary of the views held at that time (1885) concerning the development and histologic structure of psoriatic lesions, the tumor in question was a squamous cell epithelioma Charache[4] reported a case of squamous cell epithelioma with no known history of the administration of arsenic, while Hovelborn[5] reported a similar type of lesion in a patient who gave a history of the ingestion of arsenic

1 Gray, A M H Brit J Dermat **23** 325, 1912

2 Fordyce, J A The Pathology of Malignant Epithelial Growths of the Skin, J A M A **55** 1624 (Nov 5) 1910 This report did not state definitely whether or not the epithelioma arose on a psoriatic patch

3 White, J C Am J M Sc **89** 163, 1885

4 Charache, H Squamous Cell Epithelioma in Psoriatic Patches, Arch Dermat & Syph **38** 241 (Aug) 1938

5 Hovelborn, K Dermat Wchnschr **101** 858, 1935

with perspiration, and shows pronounced, more or less sharply defined erythema and mild hyperkeratosis The erythema also involves the dorsal aspect of the terminal phalanges of the hands and tips of the toes At times the volar surface of the fingers shows some maceration Occasionally the hands are dry They are always warm at room temperature The skin of the body is normal The anterior aspects of the legs are shiny and dry On the buttocks are remnants of a diaper rash The nails of the feet and hands are normal There is complete development of the deciduous teeth, which are, however, small The blood pressure could not be felt The radial pulse returned at 90 Her intelligence is that of a high grade or borderline defective

Roentgenograms taken at Babies Hospital showed the cranial cavity to be small and, in relation to the face, suggestive of cerebral hypoplasia The bone maturation is normal, however, there is osteoporosis of all bones, and severe coxa valga is present

Results of laboratory examinations were as follows Arsenic was 0 12 mg per hundred cubic centimeter, dry blood serum albumin 5 61, serum globulin 2 47, nonprotein nitrogen 32, plasma chlorides 107, and fasting blood sugar 80

A complete blood cell count showed a hemoglobin of 84 per cent, red blood cells 4,420,000 and white blood cells 9,000, with polymorphonuclear leukocytes 69, monocytes 5, lymphocytes 22 and eosinophils 4 In later counts the monocytes and eosinophils amounted to 1 per cent only

Results of tuberculin tests with dilutions of 0 01 and 0 1 intradermally were negative The Kline reaction was negative Urinalysis revealed no sugar, there was a faint trace or no albumin

DISCUSSION

Dr David Bloom In my opinion this is a case of minor ectodermal dysplasia The child has keratosis palmaris et plantaris, hypotrichosis and small teeth Involvement of the sweat glands would make it a major ectodermal dysplasia, which differs from the minor one in this and also in regard to the mode of inheritance

Dr E W Abramowitz I also think that this belongs in the group of ectodermal defects, but that it is different from the anhydrotic type

Dr A Benson Cannon We all thought it more likely an ectodermal defect, for the reasons enumerated by Dr Bloom and Dr Abramowitz I believe that the patient has been studied in the Babies Hospital and that the opinion of the pediatricians was that she had an ectodermal defect

Dr Paul Gross To rule out the possibility of acrodynia I referred the patient to Babies Hospital This diagnosis was considered because of the intense redness of the palms associated with excessive sweating The keratosis of the plams and especially the absence of neurologic symptoms were against the diagnosis of acrodynia

Dr Helen O Curth The child has no pains in the arms and hands, and this would also speak against acrodynia She has no ectodermal defect She perspires normally and suffers from increased perspiration of the palms and soles The teeth are small but complete Ectodermal dysplasia would affect only male subjects She does not suffer from the type described by McKay and Davidson, which shows disturbance of the nails and hair and which occurs in men and women In this case there is no heredofamilial involvement The child has a few signs which are seen in Werner's and Rothmund's syndromes (Thannhauser, S J *Ann Int Med* **23** 559 [Oct] 1945), especially some defects of the germ plasm She has, however, no cutaneous changes, such as

PARAFAVUS RESTRICTED TO THE SCROTUM

Report of a Case

EDWARD P CAWLEY, M D
AND
ROBERT H GREKIN, M D
ANN ARBOR, MICH

Although most dermatologists in this country know of favus and are familiar with its manifestations, relatively few of them have been afforded an opportunity to see or study a case of parafavus or pseudofavus



Two views of the scrotum, showing numerous scutula These were composed exclusively of filaments and spores

Favus, a recalcitrant, inflammatory fungus-instigated cutaneous eruption which may involve the scalp, glabrous skin and nails, is endemic in Eastern Europe Yellow, cup-shaped crusts, or scutula, are a spectacular, though not invariable, feature of the disease Achorion schoenleini is the classic etiologic agent, the

From the Department of Dermatology and Syphilology, University of Michigan Medical School

gland duct A few cells had the appearance of grains in corps ronds Multilocular lacunas had formed beneath these dyskeratotic masses The corium was edematous and infiltrated by numerous lymphocytes The condition was diagnosed as Darier's disease

The serum cholesterol was 229 mg per hundred cubic centimeters The result of the cephalin flocculation test was negative

The patient has been taking 100,000 units of vitamin A per day, combined with 15 Gm of soybean lecithin, and there has been considerable improvement The eruption on the neck and shoulders, arms and chest has almost completely disappeared, and the itching has entirely subsided, as manifested by the absence of excoriations The hyperkeratosis of the palms has diminished, but the flat warts are still present The remaining lesions on the abdomen appear less inflammatory, but show the clinical characteristics of keratosis follicularis

DISCUSSION

DR FRED WISE I accept the diagnosis on histologic grounds if they are characteristic, but I must admit that clinically I would be inclined to hesitate about the diagnosis with a short observation period The lesions on the hands more closely simulate epidermodysplasia verruciformis In order to obtain a histologic picture of Darier's disease in this patient it would be desirable to remove a lesion from the trunk, rather than from any other part of the body I would say that clinically it was atypical Darier's disease

DR SAMUEL M PECK If a case of Darier's disease is followed over a period of many years one begins to understand, perhaps, dermatoses to which we give a name, but about which we know little I could show true cases of Darier's disease in which individual lesions around the mouth and eyelids look like seborrheic dermatitis, for instance I have seen patients with Darier's disease which is apparently under control and quiescent suddenly show an eruption which looks like benign familial pemphigus after exposure to ultraviolet rays It seems to me that corps ronds are not the most important characteristic histologic feature The characteristic feature of Darier's disease is its wetness or subepidermic vesicle formation If one begins to give large doses of vitamin A, the first thing that disappears in active disease is the wetness, and then the corps ronds and grains disappear Dyskeratosis in itself is not characteristic of Darier's disease because it occurs in other types of pathologic processes, but I do not know of this tendency to wetness, i e, edema plus corps ronds, in any other disease There is much that we do not know about Darier's disease, that there is a low blood level of vitamin A and that it takes an unusually large amount in some cases to bring this up to normal, that in these cases it seems that provitamin A is not metabolized and that there may be night blindness, do not explain all of the cases The patients are sensitive to light at some time I would like to point out that in a number of cases in which the administration of vitamin A was rushed, improvement occurred only when therapy was discontinued for a while There can be too much of a good thing in treatment

DR PAUL GROSS Dr Wise's skepticism as to the diagnosis can be explained by the success of treatment Before treatment was begun, the eruption was more widespread and, especially around the hair line and on the neck, it resembled seborrheic dermatitis The eczematous appearance was further enhanced by the presence of many excoriations The disappearance of the eruption, except for the discrete papules on the chest and abdomen, and the decrease in the thickness of the palmar keratosis signified the improvement following treatment

News and Comment

GENERAL NEWS

Pacific Dermatological Association Organized—As early as May 10, 1938, the Los Angeles and San Francisco Dermatological Societies began holding combined annual meetings These meetings were not held regularly during the war but were resumed directly after the war ended To meet the need for a more formal organization the Pacific Dermatological Association has been organized It is open to the members of the Los Angeles, San Francisco, San Diego, Pacific Northwest and Rocky Mountain dermatological societies and to all other properly qualified dermatologists in the western portion of the United States, including California, Oregon, Washington, Nevada, Idaho, Utah, Arizona, Montana, Wyoming, Colorado and New Mexico, in British Columbia and Alberta, Canada, and in Alaska, Hawaii and Mexico

The present officers are as follows president, Samuel Ayres Jr , Los Angeles, vice president, Leon Frank Ray, Portland, Ore , secretary-treasurer, H V Allington, Oakland, Calif , and assistant secretary, Walter R Nickel, San Diego, Calif

The next meeting will be held at the Hotel del Coronado, Coronado (San Diego), Calif , on Aug 5 and 6, 1949 It will consist of a clinical session, symposiums and presentation of scientific papers

Revised Edition of Motion Picture Reviews Now Available—The Committee on Medical Motion Pictures has completed the first revised edition of the booklet entitled "Reviews of Medical Motion Pictures" This publication now contains all the film reviews published in *The Journal of the American Medical Association* up to Jan 1, 1949 It also includes a classified table of contents as well as a list of motion pictures available through the Motion Picture Library of the American Medical Association

The purpose of the reviews is to provide a brief description and evaluation of motion pictures which are available to the medical profession Each film is reviewed and commented on by competent authorities

Copies are available on request from the Committee on Medical Motion Pictures, American Medical Association, 535 North Dearborn Street, Chicago 10

Bronx Dermatological Society.—On May 19, 1949, the Bronx Dermatological Society celebrated its twenty-fifth anniversary at a dinner held at the Hotel Barbizon Plaza, New York

DR DAVID BLOOM I agree with what Dr Wise has said The blackish plaque on one leg is undoubtedly the result of an old dermatitis hemostatica and varicose ulcer The general eruption, which is of recent origin and followed pneumonia, is unquestionably lichen planus

DR CHARLES S MILLER From the photomicrographs I think that lichen planus can be definitely ruled out I cannot rule out the possibility of dermatitis hemostatica Dr Bernstein tells me he did the Perles' stain and got a positive reaction To me, that plus the fibroblastic reaction and angioblastic proliferation would indicate the inflammatory stage of Kaposi's sarcoma I had 1 case in which there were lesions of twenty years' duration which still showed the early signs of the inflammatory stage

For purposes of description, the histologic changes of Kaposi's sarcoma can be divided into the following stages (1) inflammatory stage, (2) angiomatous stage, (3) angiosarcomatous stage and (4) sarcomatous stage The photomicrographs in this case are consistent with the clinical diagnosis of Kaposi's sarcoma in the inflammatory stage Blue nevus is a lesion in which one sees connective tissue cells producing pigment Apparently this patient has lesions of Kaposi's sarcoma in the inflammatory stage and a blue nevus

DR DAVID BLOOM I was told that the biopsy specimen was taken from the old hemostatic scar on the leg This would explain the diagnosis of Kaposi's sarcoma as made by the pathologist A biopsy specimen from one of the lesions on the body would surely reveal the structure of lichen planus

DR EUGENE T BERNSTEIN The interesting feature is the coincidence of Kaposi's sarcoma with a pigmented nevus which proved to be a typical blue nevus which has nothing to do with the Kaposi's sarcoma We know today that hemorrhagic tumors may exist in the viscera without having been suspected In this case a pulmonary infection existed but was proved to be not a Kaposi's sarcoma involvement To me the diagnosis is unequivocally conclusive, verified by Dr Sachs's histologic examination The histologic features are so typical for Kaposi's sarcoma that they cannot be mistaken for any other disease

Steatocystoma Multiplex in a Negro Woman Aged 23 Presented by DR FRANK VERO

Herman Sharlit, M D, *Chairman*

Maurice J Costello, M D, *Secretary*

May 7, 1946

Verruca Acuminata of the Penis Simulating Carcinoma Presented by DR S IRGANG

Erythema Annulare Centrifugum Presented by DR ANDREW H MONTGOMERY

L G, a man aged 42, registered at the department of dermatology and syphilology, New York Polyclinic Medical School and Hospital on July 2, 1945, with a recurring and ever changing eruption of eight years' duration The appearance then was similar to that at present, but the eruption was more extensive in distribution and more bizarre in character The patient had been attending another clinic for a few months previously, where he had received autohemotherapy and injections of bismuth compound Results of mycologic examinations then, as now, were negative The blood and urine showed no abnormality Except for an occasional cold he had enjoyed good health

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

Lewis B Robinson, M D, *Chairman*

Samuel M Peck, M D, *Secretary*

April 2, 1946

Juvenile Xanthoma in an Infant Girl Aged 4 Months Presented by Dr Charles S Miller

DISCUSSION

In discussing juvenile xanthoma the question comes up as to whether the condition is juvenile xanthoma or nevoxanthoendothelioma There was no evidence in the slides of involvement of the blood vessels or of endothelial proliferation McDonagh in 1912 described 5 cases and used the term nevoxanthoendothelioma because he held the belief that some of the cells of the cellular mass were derived from the endothelial cells of the blood vessels Senear and Caro reviewed the literature in 1936 and reviewed the cases of McDonagh The histologic pictures in their cases fitted in with those described by McDonagh They did not believe that any of the cells of the cellular mass were derived from the blood vessels, but from the reticuloendothelial system I think that there is no question from the histologic examination in this case as to the diagnosis of juvenile xanthoma

Progeria (?) with Erythema of Hands and Feet, Partial Alopecia, Congenital Coloboma and Osteoporosis Presented by Dr Helen O Curth

E H, a white girl aged 6, is the second child of five All other children and the parents are healthy, and there is no consanguinity of the parents The child was delivered normally At birth she showed a coloboma of the iris and choroid of the left eye and esotropia She walked at the normal time, and dentition began at 8 months Speech was delayed until she was 2½ to 3½ years old Her hands and feet were red at birth Intensification of the redness, desquamation and extreme perspiration of the palms have been observed for the past year The child complains of pain in the hands in cold weather Diffuse alopecia has existed since birth

In 1945 resection of the external rectus and recession of the left internal rectus was performed in the Institute of Ophthalmology, and at Babies Hospital a biopsy of the skin of the left thigh was performed for changes showing reddish-purplish discoloration No diagnosis had been made before this, and the biopsy was inconclusive The sweat glands and dermal appendages were found to be normal There is enuresis nocturna, and polyuria is rather pronounced during day, but there is no excessive drinking The child has a craving for salt

Examination shows a small child with pale facial skin, giving her the expression of an old woman The hair of the scalp is sparse and fine, and there is diffuse partial alopecia A coloboma of the left eye is present The liver and spleen are palpable The skin of the palms and soles is at times moist, dripping

With treatment with pragmatar,® containing coal tar distillate, colloidal sulfur and salicylic acid, almost the entire eruption cleared The patient stated that he notices some perspiration on the body He now presents palmar and plantar hyperkeratosis and on the legs several well defined slightly scaly patches with a somewhat raised border The finger nails are yellowish (they are regularly scraped down by the patient) The toe nails show the same discoloration and onychogryphosis (This case has been published in detail in ARCH DERMAT & SYPH **56** 834, 1947)

DISCUSSION

DR DAVID BLOOM When observed at the Skin and Cancer Clinic a few years ago, this patient did not present the well defined scaly plaques shown on the photographs here He showed thickened reddened hyperkeratotic skin on the abdomen, lower part of the back, knees and wrists, with keratosis palmaris et plantaris At that time this disease, which has been present since early childhood, was diagnosed as congenital erythroderma ichthyosiforme, in which group it fitted best The mycotic infection which has developed was unquestionably superimposed on the original disease

DR ROYAL M MONTGOMERY The presenter has had an excellent result so far in this patient Lesions on the glabrous skin caused by Trichophyton purpureum respond much more quickly than those on the palms and soles Any strong fungicidal remedy will clear up the glabrous skin However, the hands and feet present a more difficult problem and it takes persistent treatment to effect any permanent improvement

DR E W ABRAMOWITZ I am sure that most of us who saw this patient at the clinic agreed that he presented a classic picture of erythroderma ichthyosiforme The photographs presented tonight of the lesions on the body certainly do not give the impression of ichthyosis of any type It is possible that a secondary fungous infection developed, but it is strange that Dr Muskatblit could not grow this organism after so many attempts

The palmar and plantar lesions seen now do not give the impression of onychomycosis, but rather of a dystrophy, with keratosis of the palms and soles

DR JESSE A TOLMACH I have seen only a few generalized T purpureum infections of the skin They are not common Though the disease responds to local applications of benzoic and salicylic acid ointment or weak tincture of iodine, there are usually recurrences

DR RUDOLF L BAER I agree with Dr Goodman that this patient is suffering from two diseases, namely, a nevoid anomaly and a generalized fungous infection We believe that the nevoid anomaly makes this patient susceptible to the fungous infection We do not think there can be any doubt that this patient had a generalized fungous infection in view of the characteristic fungous mycelia found in almost all the scrapings taken from many different areas The patient stated that two days after starting to use a tar-sulfur-salicylic acid preparation the eruption began to disappear From histologic examination of tissue from the back the disease was diagnosed in 1944 as characteristic of erythroderma ichthyosiforme congenitale, although that diagnosis was not upheld by our own observations at any time The man undoubtedly has a nevoid anomaly, and our assumption is that the tendency of this patient to have a generalized infection with T purpureum is due to this congenital anomaly The patient stated that he never perspired below the neck up to the time the eruption disappeared, since then he has begun to perspire in the armpits and on the chest We expect to study the patient's

scleroderma or atrophic dermatosis, and no diabetes, and there is no family history of the disease The syndrome she exhibits fits into that of progeria of children, with the facial expression of an old woman, shortness of stature, osteoporosis and joint deformity I would also like to point out that the child has a craving for salt and has low blood chlorides These two features would point, perhaps, to some insufficiency of the adrenal cortex Studies to determine whether there are any changes in the heart or vascular system will also have to be undertaken

Purpura Annularis Telangiectodes Presented by DR EUGENE F KELLEY

A L, a white widow aged 41, is presented from the Vanderbilt Clinic with an eruption on the hips and legs, of about two months' duration The lesions began as small red spots that increased in size They were distributed symmetrically and did not itch The individual lesions were oval, from dime-sized to dollar-sized macules, bluish red, nonpigmented and telangiectatic and did not disappear on pressure New lesions have appeared since that time on all the extremities and on the trunk The older lesions have assumed annular form, clearing in the center with red spots on the borders There is considerable hyperpigmentation in the older lesions In 1933-1934 the patient was treated for pulmonary tuberculosis which was said to be arrested

The Wassermann reaction of the blood was negative, and the blood cell count and urine were normal The coagulation time was 4 minutes, 10 seconds and the bleeding time 2 minutes, 3 seconds The result of the tourniquet test was negative The blood pressure was 162 systolic and 70 diastolic

Biopsy showed a diapedesis of red blood cells with inflammatory reaction, and slight thickening of capillaries The sections showed purpura, and the changes were consistent with a diagnosis of purpura annularis telangiectodes (Majocchi)

DISCUSSION

DR MAURICE J COSTELLO I think that most of the clinical features are lacking in the eruption which this patient presents, such as punctuate purpura, hyperpigmentation, a tendency to annular formation and scarring

Acanthosis Nigricans (?), Follicular Dermatitis of the Back, Latent Syphilis, Adenoma of the Thyroid Gland Presented by DR HELEN O CURTH

Keratosis Follicularis Presented by DR PAUL GROSS

A R, a Cuban woman aged 33, has had a generalized cutaneous eruption since childhood When first seen at the Vanderbilt Clinic, on Jan 28, 1946, the eruption was present on the face, neck, abdomen, back and upper extremities The lesions were discrete and acuminate red hyperkeratotic papules There was some scaling on the neck, and many of the lesions were excoriated On the dorsum of the hands and feet and on the wrists were many flat papules resembling juvenile warts There was a diffuse yellowish keratosis of the palms Close inspection revealed the presence of minute pores producing a resemblance to the hyperkeratotic lesions on the palms and soles seen in parakeratosis There was circumscribed keratosis on the soles

Biopsy of a section from the chest disclosed several isolated lesions These were characterized by the formation of a plug of epithelial cells keratinized with retained nuclei At least one of these proved to be at the orifice of a coil

miliaris disseminata faciei heal with great difficulty in the Negro I have not seen the eruption resolve entirely in any case, even after a year or more of observation

Multiple Tuberculids, Lichen Scrofulosorum Now Present Presented by Dr Louis Tulipan

DISCUSSION

Dr Marion B Sulzberger We all know that the tuberculoderms, in all their various forms and combinations, are much commoner in the Negro than in the white population and that, in particular, the transitional forms between the different kinds of tuberculoderms, including lupus, tuberculids and sarcoids, as well as tuberculosis of the soft parts, are commoner in the Negro I should like to call attention to the most successful measures of treatment of lupus vulgaris and scrofuloderma introduced by Charpy in France in 1941, which were first published in 1943 Charpy's results were simultaneously and independently confirmed by the studies of Dowling and his co-workers in England These measures consist of the administration of large doses of vitamin D_2 by mouth, plus a supplement of small doses of calcium salts by mouth or simply milk by mouth According to reports, this treatment has radically improved the prognosis in many cases of severe lupus vulgaris 80 or 90 per cent of the lesions disappear with this treatment This therapeutic approach and its results perhaps throw some light on why there is more tuberculosis among Negroes than among white persons, because, of course, the vitamin D formation in the average Negro skin is likely to be less than in the white Moreover, the diet of the Negro is often apt to be lower in vitamin D-containing foods and calcium, so that perhaps the success of this form of therapy and the higher incidence of cutaneous tuberculosis and the many diverse forms of tuberculosis in the Negro are related I should like also to call attention to the theory (as already pointed out by both French and English schools) that older and more difficult dietary forms of treatment for tuberculosis, namely, salt-poor diets and vitamin additions as suggested by Gerson, Hermannsdorfer and Sauerbruch, are effective actually because of the large amounts of calcium and vitamin D_2 which they contain It seems to me that this new therapy may be a superior and more sharply focused method of accomplishing the same effects At any rate, the Charpy-Dowling method is well worth trying in all forms of cutaneous tuberculosis and in tuberculosis of the subcutaneous structures and of certain viscera I hope that it may also find some use in selected nontuberculous diseases

Dr Samuel Irgang I was under the impression that the greater frequency of tuberculids in the Negro was due to the higher incidence of tuberculous disease associated with lowered resistance Its relation to a deficiency of vitamin D_2 in the skin is most interesting

Dr Louis Tulipan The interesting thing about this patient is the fact that he had various manifestations of his tuberculosis on the skin He had previously had erythema induratum, which had healed, then papulonecrotic tuberculids, the scars of which he shows on the extremities Recently lichen scrofulosorum developed A week ago there developed tiny white, shiny, discrete papules closely aggregated on the side of his neck, which fit well into the picture of lichen nitidus It is certainly interesting that in one patient there may be found these various manifestations of the disease

A Case for Diagnosis (Mycosis Fungoides? Dermatitis Herpetiformis?) Presented by Dr Frank C Combes

Because of the effect of excessive doses of vitamin A mentioned by Dr Peck, I decided to use smaller doses of the vitamin and tried to enhance its absorption and utilization by the addition of soybean phosphatides A decided effect of lecithin on vitamin A absorption in human beings has been demonstrated by Adlersberg and Sobotka *(J Nutrition* **25** 255 [March] 1943) The clinical result in this case of Darier's disease indicates that the simultaneous administration of soybean lecithin and vitamin B complex with moderately high doses of vitamin is of definite value

Psoriasis, Xanthelasma, Xanthoma of Tendon Sheaths Presented by DR BEATRICE M KESTEN and DR PAUL GROSS

Lichen Planus of Mouth (?), Xanthoma of Eyelids and Tendon Sheaths (Associated with Hypertensive Cardiovascular Disease), Familial Type Presented by DR PAUL GROSS and DR BEATRICE M KESTEN

Kaposi's Sarcoma Coincidental with Pigmented Nevus Presented by DR EUGENE T BERNSTEIN

R M, a man aged 51, was admitted to Beth David Hospital in February 1946, acutely ill, with a temperature of 105 F A diagnosis of lobar pneumonia of the right lung was made The white blood cells numbered 21,000 on admission, with subsquent cell counts of 17,000, 10,000 and 7,500 Sulfadiazine was administered for seven days, but, as the temperature did not fall below 104 F, penicillin was then employed A roentgenogram showed pneumonic consolidation

There is boardlike, blackish brown infiltration of the right leg with ulcerations, pigmented nodules in the vicinity and many infiltrated pigmented spots on the entire trunk, with some infiltrations on other parts of the body A pigmented nevus is present on the right arm The eruption has existed for five or six years but has caused no discomfort, pain or itching The cutaneous changes were regarded before admission as varicose veins stasis dermatitis, and the ulcerations were ascribed to an injury

A biopsy specimen from the leg showed numerous dilated blood vessels throughout the cutis and particularly the upper part of the cutis Many of them were filled with blood elements There was a diffuse cellular infiltration The overlying epidermis was thin and flattened The rete pegs were missing The palisade layer was intact and contained considerable pigment There were no other important changes in the epidermis The cellular infiltration was composed of small round cells, wandering connective tissue cells, few angioblasts and spindle cells There was some hemorrhage and pronounced pigmentation The result of Perles' test was positive The diagnosis was Kaposi's sarcoma

A dime-sized elevated pigmented spot was excised from the right arm for biopsy In the middle part of the cutis there was a small mass consisting of cellular elements and some pigment There were no important changes in the surrounding cutis The cells composing this mass were largely spindle shaped, with oval vesicular nuclei, and contained pigment These were connective tissue nevus cells Perles' reaction was negative The diagnosis was blue nevus

DISCUSSION

DR FRED WISE I was under the impression that several lesions on the shin were elements of pigmented, annular and atrophic lichen planus I suggest that a biopsy specimen be taken from a lesion on the skin about 4 inches (10 cm) below the patella

have been described I have not seen the eruption around the mouth, affecting the vermilion surface and the skin below it If the patient is not exposed to the drug again, the pigmentation resumes a normal appearance in time

The other question raised by Dr Vero was whether it is correct to call this type of reaction a fixed eruption I think that it is correct, because the term fixed eruption refers to any cutaneous manifestation that may appear as long as the eruption recurs at the exact site of a previously affected area This patient took 2 tablets of a preparation which contains a mixture of the yellow and white forms of phenolphthalein It would not matter whether he took the yellow or white variety of the drug, as either would cause an exacerbation He should be questioned as to whether he is taking barbiturates or any other of the fourteen or fifteen drugs capable of producing fixed eruptions The patient may experience sensitivity to other drugs, such as the barbiturates or, as in one interesting case, to magnesium hydroxide

DR FRANK VERO I thought that the pigmentary changes, and especially the depigmentation, were rather unusual When first seen the patient presented a clinical picture of herpes labialis or an actinic dermatitis possibly secondarily infected He denied exposure to sunlight but admitted having taken ex-lax® as a cathartic I was hesitant to diagnose the disease in this case as a fixed eruption because of the inflammatory changes which preceded the pigmentation and depigmentation I am glad to be enlightened by Dr Abramowitz that eruptions of this type can be considered as fixed eruptions, although at many of our section meetings somewhat different views have been expressed by experienced dermatologists I should like to add that the exacerbation which the patient presented tonight on the wrist appeared after the ingestion of 2 tablets of ex-lax® (a laxative containing phenolphthalein) this morning

Boeck's Lichenoid Sarcoid, Iridocyclitis, Ptosis Presented by DR MAURICE J COSTELLO

L R, a Negro aged 24, is presented from Bellevue Hospital with a generalized eruption The patient was well until nine months ago, at which time there developed an eruption of the legs, which gradually spread to involve the whole body About the time the eruption appeared, the patient had a "cold," which has persisted to date There was no pruritus until two weeks ago, when itching became intense Three months after the appearance of the eruption the patient experienced iridocyclitis of the left eye, for which he received penicillin at another institution He has lost 30 pounds (14 Kg) in the past year

The lesions, consisting of papules and plaques, violaceous to brown and infiltrated but freely movable in the skin, are present on the extremities, face and trunk There is generalized adenopathy, the spleen is palpable 3 fingerbreadths below the costal margin, the right testis is atrophic, and there are changes in the left eye compatible with iridocyclitis Respiratory excursions are limited on both sides, but particularly on the left

The red blood cell count was 4,130,000, with hemoglobin 13 Gm per hundred cubic centimeters, the white blood cell count was 7,650, with 61 per cent polymorphonuclear leukocytes, 7 stab forms, 31 lymphocytes, 2 monocytes, 2 eosinophils and 1 basophil The urine was normal The total protein in the blood was 8 1 Gm, with albumin 3 1 and globulin 5 0 Gm The cephalin flocculation result was 4 plus, the icteric index 8 8, cholesterol 154 mg, nonprotein nitrogen 28 mg per hundred cubic centimeters, sugar normal, chlorides 500 mg per hundred cubic centimeters and vitamin C 0 58 mg per hundred cubic centimeters The result of the Mazzini

The eruption began on his arms and spread to the legs The face and trunk have been comparatively free At present it is mainly confined to the legs and consists of rather firm nodules which spread peripherally to form rings, one border of which becomes incomplete, forming festoon-shaped patches Resorption of part of the ring and coalescence of patches give geographic forms At present there is one complete ring and several partial rings with spreading elevated borders and nearly normal centers There are no vesicles, only slight scaling, and no subjective symptoms The eruption is not seasonal

The patient returned to the clinic on March 22, 1946, with the present outbreak He stated that after his first visit he was well for four months At that time he was given a mixture containing powdered rhubarb, sodium bicarbonate and cascara in peppermint water He reported that in times past he had clear periods of a month or so A recent attack of influenza with fever caused no change in the eruption

DISCUSSION

DR CHARLES WOLF A definite diagnosis in these cases is difficult in the early stages The lesions simulate other diseases Over a period of years these lesions persist and transmute into a well recognized entity It is well to bear in mind that this eruption lasts for many years as an innocent disease and then develops into a lymphoblastoma The disease in this case has some of the early earmarks of mycosis fungoides

DR E W ABRAMOWITZ I do not recall any case of erythema annulare centrifugum that turned out to be mycosis fungoides My patients responded to intramuscular injections of a bismuth preparation, but cure is not permanent

DR BEATRICE M KESTEN I have never cured one of these patients, but I have never tried a bismuth preparation I think that histologic examination would differentiate erythema annulare centrifugum from mycosis fungoides d'emblée

DR DAVID BLOOM This patient was treated at the Skin and Cancer Clinic with injections of bismuth compound and benefited greatly, although some lesions have reappeared The diagnosis of erythema annulare centrifugum was made This belongs to the large category of erythema multiforme In the persistent type of the disease, bismuth compound has proved more effective in my experience than any other remedy

DR ANDREW H MONTGOMERY I am sorry that this patient could not have been shown six weeks ago I have gone through the literature of the last ten or twelve years rather carefully, and there has been no mention of the development of lymphoblastoma of any sort To quote Dr Michelson, "There are many forms of this disease, and very little is known about it"

Generalized Dermatomycosis (Trichophyton Purpureum) Associated with Hyperkeratosis Palmaris et Plantaris Presented by DR RUDOLF L BAER and DR EMANUEL MUSKATBLIT

A R, a man aged 25, was previously presented before this section on Feb 1, 1944, with a diagnosis of erythroderma ichthyosiforme congenitale (ARCH DERMAT & SYPH **51** 161, 1945) He has had an eruption on the hands and feet since birth and on the body since the age of 13 or 14 He stated that he did not perspire except on the face and scalp The p_H of the skin of the face and ear area varied between 4 2 and 4 5 and of the rest of the body between 4 3 and 6 5, with the majority of values lying between 5 0 and 6 0

miliary sarcoidosis It is difficult to differentiate among sarcoidosis, pneumonoconiosis, acute miliary tuberculosis and carcinomatosis in roentgenograms of the chest

A Case for Diagnosis (Dermatitis Medicamentosa?) Presented by DR LOUIS TULIPAN

P C, a woman aged 60, born in Russia, is presented from Bellevue Hospital with an eruption on the left leg of two years' duration The patient presents two quarter-sized bullae arising from normal skin on the anterior aspect of the lower third of the left tibial region There are small erythematous papules surrounding the bullae The bullae are turbid and almost solid in character and do not exude fluid when punctured with a needle The lesions were first noticed in June 1944, after a pruritic papular eruption in that area The lesions disappear sporadically, only to recur They are clear when they first appear, but become cloudy after a few days

The patient's past history and family history are irrelevant

In June 1946, she was hospitalized She was found to be sensitive to soap, plaster and sunlight A culture of the bullae contents in April 1946 grew gram-positive rods, and the smear showed 24 per cent eosinophils The urine has always been normal Culture of bullae contents in June 1946 grew Staphylococcus aureus and diphtheroids A smear of the contents September 30 showed no cells The results of a complete blood cell count were normal

DISCUSSION

DR E W ABRAMOWITZ I am sure that if the patient gave a history of having taken bromides Dr Tulipan would consider the eruption a bromoderma I think that she presents a bromoderma, as her denial of medication is too vehement It is possible that she is getting the bromide or iodide in some other form, as in food I would wait until the lesions subside and then watch for a recurrence with a test dose of a bromide or iodide

DR ISADORE ROSEN Another possibility which must be taken into consideration is that of contact dermatitis Occasionally one sees patients who experience local reactions of a vesicular and bullous nature due to shoe dyes

DR LOUIS CHARGIN I would agree with the diagnosis of bromoderma if a history of the ingestion of the drug could be obtained Is it pertinent to ask whether bromides produce fixed eruptions? The process may be an artefact, and its persistence in the same spot would favor an artefact as against bromoderma

DR FRANK C COMBES When one sees a bizarre eruption for which one cannot give a definite diagnosis, it is always customary to consider an artefact or an eruption due to drugs, and I think that one or the other is the most likely diagnosis here I favor an eruption due to drugs, and I agree entirely with Dr Abramowitz There are two types of eruptions due to the halogens one due to their cumulative effect and the other to sensitivity Sensitivities due to the halogens are unusual and may be serious Fatalities have been reported The tendency in this case for the eruption to recur in a fixed location without any history of ingestion of bromides is evidence in favor of an unusual sensitivity to bromides, and I also agree with Dr Abramowitz that the only real test would be the administration of bromides One cannot determine by ordinary tests or blood estimations whether an eruption is due to bromides, because cutaneous and even nervous lesions due to bromides are not necessarily dependent on the amount present A patient may have a large amount of bromides in his system without any evidence of bromism, whereas in other instances an infinitesimal quantity will produce symptoms I feel that the

sweat output to see whether there is any objective evidence of an anomaly of the sweat mechanism

DR EMANUEL MUSKATBLIT I believe that this case is interesting from several points of view First of all, it is a generalized dermatomycosis Large areas of the trunk and extremities were formerly affected Now there is no eruption on the trunk and only a little involvement of the right leg, but both hands and feet and all finger nails and toe nails are still affected Dr Baer obtained cultures from a lesion on the neck which showed T purpureum I saw the patient later and took several scrapings from the wrists, palms, thighs, toes, soles, finger nails and toe nails All specimens contained fungi of the pathogenic type in microscopic preparations Cultures were made in twenty-one tubes, and all were overgrown with saprophytic organisms, so that we were unable to obtain the pathogenic species I believe with Dr Baer that the erythematosquamous lesions and the changes of the finger nails and toe nails are due to a fungous infection which developed on the basis of a preexisting anomaly of the skin, though what the relationship is would be difficult to say Ichthyotic skin presents a mass of scales on the surface which may be a good soil for the propagation of fungi On the other hand, the dry skin is unfavorable for the growth of fungi, but the lack of sweat with its chemical substances inhibiting the fungi is again favorable for their propagation It is worth while mentioning that we did not obtain cultures of T purpureum from all lesions We assume, however, that all the lesions we have seen and see now are at least partially due to fungous infection, in this instance T purpureum This is considered a highly resistant fungus, but the eruption on the trunk has cleared up in a short time, so that it seems that not all cases of T purpureum infection are as resistant as some reports would have one believe

Tuberculosis Colliquativa of the Ankle Presented by DR S IRGANG

Dermatitis Medicamentosa (Atabrine), Lichen Planus, Atrophy, Scars, Alopecia, Pigmentation, Nail Changes Presented by DR ANDREW H MONTGOMERY

Lymphangioma Circumscriptum of the Knee, Thigh and Abdominal Wall Presented by DR S IRGANG

Herman Sharlit, M D, *Chairman*

Maurice J Costello, M D, *Secretary*

Oct 1, 1946

Micropapular Tuberculid Presented by DR S IRGANG

Tuberculosis Miliaris Disseminata Faciei Presented by DR S IRGANG

DISCUSSION

DR SAMUEL IRGANG Negroes are generally more sensitive to tuberculin than are white patients In this disease the Negro usually reacts locally to an intracutaneous injection of 0 1 cc of old tuberculin in a dilution of 1 1,000, and positive reactions with a dilution of 1 10,000 are not unusual The lesions of tuberculosis

erythematous scaling and fissuring circular patch In November 1939, the patient noted an erythematous circular patch at the corner of the mouth which steadily grew, so that in one month it involved the entire chin and the area around the mouth and was eczematous Lesions have persisted at the left angle of the mouth and the right side of the chin, with a tendency to fissuring

Patch tests with cosmetics resulted negatively Results of various patch tests with feathers, grasses and animal hair were also negative Positive reactions were obtained with scratch and intradermal tests of the following substances camel hair, chicken feathers, duck feathers, goose feathers, goat dander, orris root, stock house dust, autogenous house dust, sheep wool, silk and cow and dog dander The result in an intradermal test with tobacco was moderately positive, but the reaction to the scratch test was negative The patient had a number of positive reactions to foods

She has been given injections of ambotoxoid for desensitization purposes and has received treatment with castellani's paint, 0 5 per cent ammoniated mercury in boric acid ointment, ten injections of colloidal manganese hydroxide, penicillin ointment (with some improvement), boiled milk given intramuscularly (five times), injections of 5 cc of Upjohn's solu-B® (in sterile powder vials, each containing 10 mg thiamine hydrochloride, 10 mg riboflavin, 5 mg pyridoxine hydrochloride, 50 mg calcium pantothenate and 250 mg nicotinamide) three times a week for twelve weeks, with no change

DISCUSSION

DR J M SCHILDKRAUT, Trenton, N J I think that the patient has a discoid type of lupus erythematosus

DR J V KLAUDER I could not make much of the eruption except that it was an eczematous type of dermatitis She has an introspective, self-analytic attitude toward the lesion I thought that there was some excoriation present There was a white area which I was not sure was atrophy It suggested some manipulation I do not mean dermatitis factitia, but perhaps a nervous picking or manipulation of the lesion, causing it to persist

DR JOHN H STOKES Years ago Pusey described in his textbook what he called resistant scaly erythrodermias of the skin, and in the last three or four years I have seen 4 or 5 cases of this disease The lesion was a refractory erosive plaque of dermatitis which simply responded to nothing A common location is around the edge of the scalp, but lesions occurred around the chin and at the angles of the mouth I saw such cases at the Mayo Clinic, and 4 or 5 in Philadelphia They are *sui generis* This woman has certain attributes of the person who presents a factitial eruption—perhaps unconsciously I was glad to hear Dr Klauder speak as he did about her attitude—the almost exhibitionistic eagerness to show the lesion and cooperate in every imaginable way She is a divorcee with a very considerable tension problem, and I think that she probably picks the lesion in her sleep On the other hand, she has pustules, which lead me to think that the process might be staphylodermic and represents one of the localized pyogen-sensitive areas which just go on producing localized infections until the whole thing becomes a fibrous inflammatory plaque Pusey's cases responded finally to one thing—treatment with Kromayer lamp—and we are now treating her with the air-cooled quartz lamp using a quartz lens Since that was started she has made a good deal of progress She has however, improved with nearly everything that has been done for her, for a while The scarlike atrophy exhibited today is new The lack of elevation is also new The lesion had been so elevated that it looked almost like a granuloma She is a little paranoid, and one hesitates to take even a punch biopsy specimen from her

Dermatitis Medicamentosa (Phenolphthalein) Followed by Pigmentary Changes Presented by DR FRANK VERO

L S, a Negro aged 37, is presented from the New York Polyclinic Medical School and Hospital with an eruption of five months' duration, located on the lips, perioral region and left wrist

The patient was seen for the first time on Aug 27, 1946, complaining of a recurrent eruption on the lips and wrist of four months' duration When questioned as to intake of drugs, he said that he had changed from salt cathartics to ex-lax® (a laxative containing phenolphthalein) within recent months There were no pigmentary changes on the lips prior to the appearance of the eruption

The upper and especially the lower lip appeared swollen, with numerous vesicular and bullous lesions and oozing denudations and covered with yellowish and hemorrhagic heaped-up crusts extending to the perioral region The tongue and buccal mucosa were clear Over the flexor aspect of the left wrist there was a half-dollar-sized, sharply outlined, reddish brown edematous lesion On the neck, chest and abdomen were scattered round and oval dark, pigmented and scaly lesions (typical pityriasis versicolor) The Wassermann and Kahn reactions of the blood were negative A week later, following treatment with penicillin ointment, the eruption on the lips and wrist cleared up except for the pigmentary changes On September 12, three days after the intake of 2 tablets of ex-lax,® the patient had an exacerbation in the form of vesicles and bullae He stated that ten minutes after he took the drug his lips became swollen and blistered At present the lips show depigmentation, more so on the lower lip, and hyperpigmentation, the latter extending to the perioral region in a semicircular outline, with similar pigmentary changes on the left wrist

DISCUSSION

DR MARION B SULZBERGER Cases of phenolphthalein eruption are beginning to belong to the rarities in clinics or offices Most patients now know, or find out before they come to the skin specialist, that it is phenolphthalein which has caused their eruption and simply stop taking the drug This is in contrast to the situation years ago when such eruptions were first described and the public and general medical profession were not as aware of the possibility of eruption from this cause I think that many of the younger men here may have seen few if any of such fixed eruptions from phenolphthalein I think that this case is instructive as to what an inflammatory process can do in the way of disturbing the pigment formation I am sure that it is not unusual for long-lasting hyperpigmentation to form as a result of certain kinds of inflammation, and the nature of the inflammatory process, its location, its mechanism and cause all have something to do with the degree and persistence of resulting pigmentation Fixed eruptions due to phenolphthalein and those from certain other drugs have a strong tendency to leave long-lasting hyperpigmentation One sees that illustrated in this case, and that is not the unusual feature On the other hand, I do not recall having seen a case of fixed eruption which has left the patchy permanent (or probably permanent) destruction of pigment which is evident here I should like to ask Dr Abramowitz and others whether they have seen such cases

DR E W ABRAMOWITZ At an exhibit of the American Medical Association I showed a photograph of a patient who presented a patch almost the size of the palm and located below the left scapula with a form of the stippled pigmentation which Dr Vero's patient shows He had had several outbreaks, and apparently the pigment reacted in this particular way These cases are unusual, though several

DR HERMAN BEERMAN This whole subject is very ably presented in the *British Journal of Dermatology* by a number of men, including Goldsmith and Robb Smith (**56** 107, 1944 and **56** 151, 1944, respectively)

Contact Dermatitis with Probable Food Sensitivity Presented (by invitation) by DR JAMES M FLOOD and DR MALCOLM C SPENCER

R N, a white woman aged 39 years, obese and normally developed, presents residua of deep seated vesicles with some evidence of pyoderma, since one week ago, on both heels The condition had its onset in August 1944, while the patient was on vacation Red scaling pruritic plaques developed on both heels The patient was wearing a pair of new shoes at the time Also a small plaque of lichenification developed on the dorsa of both feet There have been recurrent vesicles since the onset of the condition Eating tomatoes has caused "hives" Drinking one glass of beer causes rhinitis

A blood cell count on April 8, 1946, revealed 72 per cent hemoglobin and 7,800 leukocytes A urinalysis resulted negatively Serologic tests of the blood for syphilis resulted negatively The serum protein and cholesterol were 6 5 Gm and 223 mg, respectively, per hundred cubic centimeters of blood The basal metabolic rate was —7 per cent

Culture for fungi produced no growth Patch tests with several different kinds of shoe leather gave positive reactions An injection of trichophytin, 1 100, yielded a positive reaction

The patient was given a trial diet plus the use locally of bland ointments Flare up occurred with the ingestion of beef, tomatoes, egg, cream of wheat and corn In our practice, trial diets are instituted after a period of two to three days' hospitalization during which time the patient is observed frequently and a base time of improvement or progression is reached During the first twenty-four hour period the patient receives nothing but water and dextrose, followed by the addition of one simple food daily In the case of this patient, after the addition of beef, which was the third day of her trial diet, there occurred a few vesicles on the soles as well as on the great toes These were interpreted as representing a flare up Within forty-eight hours it was possible to add a new food, and this was continued until tomatoes were introduced into her diet, which produced an urticaria-like reaction on the arms as well as the feet The patient was discharged from the hospital on a basic diet and asked to continue adding new foods as she had done in the hospital With the addition of eggs to her diet, a decided flare up occurred, which necessitated rehospitalization because of the secondary infection which developed During the second hospitalization, it was found, after a base line had again been reached that vesicular flares were produced by cream of wheat and corn

DISCUSSION

DR JAMES M FLOOD This patient well illustrates the etiologic difficulties that one finds in recurrent vesicular dermatitis of the hands and feet She was found sensitive to her footwear, and even when she stopped wearing shoes to which she was sensitive she continued to have vesiculation on the feet, although she was somewhat improved At some time she has had a fungous infection with sensitization as evidenced by the trichophytin test In cases of this kind it is important to differentiate the new vesicles from the old ones when one is determining the food allergies This woman has been tested for sensitivity to foods by giving her one food a day In addition to the food allergy and the contact factor, she is very

test was negative The erythrocyte sedimentation rate was 23 mm per hour The skin did not react to 1 0 mg of old tuberculin Roentgenographic examination of the chest showed numerous miliary pea-sized nodules uniformly distributed over both lung fields, compatible with the diagnosis of Boeck's sarcoid Results of roentgenographic examination of the bones were normal Histologic examination of a cutaneous lesion showed numerous tubercles composed of epithelioid cells, located within the corium, chiefly about the hair follicles and sweat glands Multinucleated giant cells were present in a few of these tubercles In one rare tubercle there was early necrosis Acid-fast stain failed to demonstrate acid-fast bacilli The diagnosis by Dr W C Von Glahn was "granulomatous lesion—either tuberculosis or Boeck's sarcoid, possibly the latter"

DISCUSSION

DR DAVID BLOOM This case represents the so-called hematogenous tuberculosis of the skin in the Negro The prognosis in this case is much better than one would think, considering the extent of the eruption and the involvement of the viscera One of the cases which Dr Mendelsohn and I reported about ten years ago was presented a few years ago at the New York Academy of Medicine, the disease cleared up entirely without any particular treatment

DR LOUIS CHARGIN I agree with the diagnosis I should like to urge an extensive trial of the Kveim test to determine whether it really has merit in the diagnosis of sarcoidosis This test is similar to the Frei test The material for the test is prepared from cutaneous lesions or affected tonsils or glands of patients with sarcoid in exactly the same way as material for the Frei test Considerable work has been done with this test in Europe, and there are a number of favorable reports I think that it should be given an extensive trial in this country

DR FREDERICK REISS In connection with Dr Chargin's remarks about the Kveim test, the literature is already extensive in the Scandinavian countries Kreim published a monograph in which he stated that in 80 or 90 per cent of cases there are specific reactions I believe that it is an important test, not only in the diagnosis of sarcoid but with respect particularly to the conflict which exists among South American dermatologists regarding the relationship of sarcoid to leprosy There is a good deal of similarity in the histologic pictures, and therefore a group of South American leprologists tried to link leprosy with Boeck's sarcoid The Kveim test definitely eliminates the controversy I think that it would be interesting to try the Kveim test in leprosy as well

DR FRANK VERO Several years ago similar cutaneous tests in sarcoid were carried out by two Boston men in a limited number of cases (Williams, R H, and Nickerson, D A Skin Reactions in Sarcoid, *Proc Soc Exper Biol & Med* 33 403 [Dec] 1935) The material used was tissue taken from sarcoid lesions and prepared as is the Frei antigen

DR MAURICE J COSTELLO Nickerson made an antigen from sarcoid nodules which when injected intradermally produced reactions in the skin similar to those obtained with the tuberculin test

When this patient was first presented at conference at Bellevue Hospital, the eruption suggested generalized lichen planus, especially since it was accompanied with severe itching I think that this patient has lichenoid sarcoid For a number of years the patient received arsphenamine therapy for syphilis

I had the impression that the arsenic therapy precipitated this eruption It seems to me that this patient may also have beginning active pulmonary tuberculosis, because of the productive cough, although roentgenograms of the chest suggest

J Schildkraut, M D, *Chairman*

Douglass A Decker, M D, *Secretary*

Sept 20, 1946

Keratoderma Punctatum of Palms and Soles Presented by DR MARJORY K HARDY and DR CARMEN C THOMAS

E S, a white woman aged 37 years, presents on the palms small, firm, horny, noninflammatory, spicule-like keratotic projections When one of the lesions is forcibly removed, a small pit remains The dorsa of the hands are normal There are similar but fewer lesions on the soles The dermatosis began when the patient was 16 years of age One sister, now dead, is said to have been similarly affected There is no history of ingestion of arsenic The Wassermann reaction of the blood was negative for syphilis

The report on the biopsy specimen was pronounced hyperkeratosis, some acanthosis and no inflammation, but some papillary spaces resembling lymph spaces, which may be artefacts The patient has received 75,000 units of vitamin A daily for five months and an emollient ointment locally There has been no change

(Hydroa Puerorum?) Urticaria Pigmentosa Presented by DR JOHN H STOKES and (by invitation) DR STEPHEN T WHELAN

C W C, a white boy aged 2½ years, presents normal skin texture with dermographism limited to areas of brown-red pigmentation which are scattered over the entire body surface The disease was present at birth The process appeared first on the face and chest as small bullae with furunculosis and then spread over the entire body, arms, legs and scalp The bullae disappeared when the patient was 3 months of age, and there have been none since The patient has wheals which leave pigmented macules Urticarial lesions always develop in areas of pigmentation, and the patient is dermographic in these spots

Calcium wafers, tincture of belladonna, 2 minims three times daily, ascorbic acid, 100 mg twice daily, and diphenhydramine hydrochloride (benadryl®), 25 mg twice daily, have been administered but the pigmentation remains unaltered Urticarial lesions are still developing, but not as strikingly as formerly

DISCUSSION

DR FRED D WEIDMAN Apparently this diagnosis is made because wheaing is present Is there anything to support that diagnosis besides the wheaing? The lesions are not yellow, as they should be, and the dermographism can be a nonspecific reaction, occurring in a variety of different dermatoses so that I do not think that this should be considered a case of urticaria pigmentosa on the evidence at hand Has the possibility of hydroa puerorum been thought of? There were vesicles and furuncles at first which would fit in with that diagnosis, together with the pigmentation and scarring which occurs in dermatitis herpetiformis

DR JOHN H STOKES I was not able to elicit any history of vesicles or pustules The fact that the eruption is limited to the covered parts of the body and the fact that the child has been exposed to the sun without unfavorable

most likely diagnosis in this case is that of bromoderma, but there are certain elements about it which make me hesitate to make any definite decision

DR HERMAN SHARLIT Has anyone attempted topical application of bromine salt?

DR E W ABRAMOWITZ I do not exactly agree with what Dr Combes said Psychiatric studies of patients admitted to mental hospitals who have been taking bromides indicate that their mental symptoms are due to long-continued use of bromides It is only when the bromide content reaches 75 mg or more per hundred cubic centimeters of serum or spinal fluid that mental bromism takes place There are patients who show a high amount of bromides in the tissue fluids who still do not show mental bromism, but the fact remains that the patients who do present mental bromism or iodism all show large amounts of those drugs in the blood The majority of patients who show mental bromism or iodism do not have cutaneous lesions Only about 20 to 25 per cent present eruptions, and they are of a comparatively minor type Apparently those patients who get cutaneous eruptions from bromides or iodides do so because of sensitivity and not from accumulation As a rule those patients do not present mental symptoms I recall only one patient, an epileptic patient who took bromides, who had an extensive cutaneous eruption, and the blood serum and spinal fluid showed large amounts of bromides That brings up the important question of salt therapy I do not believe that one should fear giving salt to patients with bromoderma or iododermas, but one should be careful when there is a large amount in the blood of patients with mental symptoms, because to further release of bromides or iodide is apt to have serious results

DR ISADORE ROSEN I should like to ask the presenter when the patient had a previous attack

DR LOUIS TULIPAN In June She was entirely well during the summer, new bullae developed two or three weeks ago

DR ISADORE ROSEN That is unusual with bromides The eruption usually persists for months I do not recall having seen this type of eruption from bromides Usually one sees nodular lesions which may ulcerate

DR FRANK C COMBES I agree with Dr Abramowitz, I did not mean to imply that mental bromism was a manifestation of sensitivity to bromides I still feel, however, that in bromism there are cutaneous symptoms which represent either sensitivity or accumulation of the drug I have observed patients with bromism who have been given sodium chloride to aid elimination of bromides, and further administration of bromides was not accompanied with exacerbation immediately, but only after the bromides had again accumulated As to Dr Rosen's remarks, I agree with him entirely that the remissions and relapses in this patient are an unusual feature It is extremely unusual for bromoderma of the granulomatous type to disappear spontaneously The lesions will persist for months, long after administration of the bromide has been discontinued In fact, this is the feature in this case that makes me doubt the diagnosis of bromoderma

DR LOUIS CHARGIN It is my impression that eruptions due to bromides are observed only as cumulative phenomena, the threshold varying so that either larger or smaller doses are required to bring out an eruption However, minute doses do not cause eruptions, as in the case of drugs that act as allergens In the case of iodides, however, a minute dose may produce an eruption and, also, the eruption may be a cumulative phenomenon

DR MAURICE J COSTELLO Eruptions due to bromides which occur on the lower anterior third of the leg are always painful, are fixed and not evanescent and are the result of accumulation of the drug in the system Bullous eruptions

DISCUSSION

DR FRED D WEIDMAN I think that all of us were struck by the unilateral distribution of the lesions Those on the face were definitely unilateral, and the ones on the loin began sharply at the line of the spinous processes The distribution was similar to that of herpes zoster This makes me wonder whether there is a congenital factor determining a distribution of that sort That is something that appears to be connected with the somites, and in the sections it seemed that these fibers were related to hair follicles, so that this disease with unilateral distribution and distribution along the somites might be a simple hamartomatous abnormality of the involuntary muscles of the hair follicles, not a true neoplasm

DR JOHN H STOKES Do any changes occur in the lesion on stroking? Is it painful?

CAPTAIN ROBERT L GILMAN Yes This man's main complaint has been one of pain, particularly on pressure and friction of the clothing We should like some suggestions as to treatment A plastic surgeon, did not think that plastic surgery would offer him very much The patient wants something done, and we were tempted to try fulguration He is genuinely disturbed by the symptoms particularly over the back

DR M H SAMITZ The lesions on the trunk were painful, he winced when I touched them, but those on the cheek were not painful and he shaves every day but complains of no pain while shaving I suggest the use of solid carbon dioxide

DR JAMES T FLOOD (by invitation) Paravertebral block might be helpful

A Case for Diagnosis (Lichen Simplex Chronicus, Lichen Planus) Presented by DR CARMEN C THOMAS

J W, a white man aged 53 years, well developed and healthy, presents a normal skin except for a lesion limited to the left buttock This is sharply circumscribed and is about the size of a large palm The upper left border seems most active and has a nodular serpiginous border with considerable induration The right upper border stops short of the gluteal cleft, which is not involved The entire right border shows considerable atrophic scarring, which is present also in the lower center of the lesion The lower outer border is scaly and at places is fissured There is scaling of the central parts of the lesion The mucous membranes are not involved The lymph nodes are normal The liver and spleen are not enlarged The cutaneous lesion has been present on the left buttock for seventeen years, beginning as a small scaling patch which gradually extended to the present size It is somewhat itchy and painful when it becomes fissured

The Kolmer and Kline reactions of the blood for syphilis were negative A biopsy specimen taken on Aug 10, 1946, was reported by Dr Beerman and Dr Weidman as representative of hypertrophic lichen planus The epidermis showed hyperkeratosis and vacuolation in the basal layers There was a densely packed infiltrate in the upper part of the corium and extending into the basal layers, composed of large clear cells, and also several areas of lymphocytic infiltrate in the corium

In the past the patient has been treated with an unknown amount of roentgen rays and by means of injections of undetermined nature Since coming under my care on August 9, local treatment has been with Pragmatar® (ointment for

face The fissure on the chin is a favorite staphylococcic location in certain types of persons who have lesions there for years and years, after every other focus has been cleared up I favor a diagnosis of resistant staphylodermia, or resistant scaly erythroderma as it was called by the older dermatologists We have included vitamins to exclude vitamin B_2 deficiency, and we have found no tuberculosis

Lupus Vulgaris Presented by DR DONALD M PILLSBURY, DR CLARENCE S LIVINGOOD and (by invitation) DR JOHN P SCULLY

A Case for Diagnosis (Histiocytoma Cutis? Calcified Cyst? Nodular Subepidermal Fibrosis?) Presented by DR REUBEN FRIEDMAN

(NOTE The histologic diagnosis of the mass from the left shoulder was "Intracystic papilloma [hard] of duct of pilosebaceous apparatus")

Reticulosis Presented by DR JOHN W LENTZ and (by invitation) DR MALCOLM SPENCER

E S, a Negro man aged 61 years, normally developed and fairly well nourished, presents residual, hyperpigmented, annular, slightly infiltrated, finely scaling plaques, the residuals of his original lesions Physical examination revealed generalized shotty adenopathy The cardiovascular, gastrointestinal, genitourinary and urologic examinations revealed no abnormalities

A complete blood cell count on Feb 13, 1946, showed 63 per cent hemoglobin, 3,100,000 erythrocytes, 4,100 leukocytes, 54 per cent neutrophils, 2 per cent eosinophils, 2 per cent monocytes and 42 per cent lymphocytes The blood sugar level and results of urinalysis were within normal limits The results of serologic tests of the blood for syphilis were negative Gastric analysis revealed no free hydrochloric acid A roentgenogram of the chest and a biopsy specimen of bone marrow showed no abnormalities

From a biopsy specimen of the skin taken on February 18 the diagnosis was "leukosis-mycosis fungoides (??)" and from a biopsy specimen of a left axillary lymph node on February 20 "reticulum cell hyperplasia"

Treatment was with roentgen rays, through thirty-five portals, total dosage varying from 300 to 1,200 r, 135 kilovolts through a 2 mm aluminum filter The individual dosage was 100 to 400 r Improvement was striking

DISCUSSION

DR HERMAN BEERMAN This patient has been presented on two previous occasions, originally with the diagnosis of psoriasis and the second time with the diagnosis of mycosis fungoides I could not reconcile the diagnosis of mycosis fungoides with the histologic sections I took the sections to Dr Weidman, who made the diagnosis of reticulosis

DR FRED WEIDMAN In a loose way, one can say that "reticulosis" is a way of getting out of the histologic diagnosis of granuloma fungoides Clinically it may be just that, and yet histologically it is not satisfactory, there is not the polymorphism of cells that one reads about in the textbooks It is hyperplasia of the reticulum and nothing else—no plasma cells and no eosinophils This serves to illustrate that there are numerous upsets of the hematopoietic system that have not been classified in the dermatologic nomenclature Every now and then one is driven to some such recourse as "reticulosis" The processes do not fit any of the accepted pigeonholes in dermatologic nomenclature, and one must give it a histologic diagnosis

The patient, who is now pale and thin, said that he was well until the present illness The medical examination revealed no abnormalties Proctoscopic examination of 25 cm of the lower bowel showed nothing abnormal and nothing apparently related to the draining sinuses, although no injection technic was employed

The blood sugar was 89 mg and the urea nitrogen 14 mg The urine was normal The serum protein was 8 0 and albumen 49 A complete blood cell count resulted in normal observations Cultures of pus were repeatedly negative for fungi on direct examination and culture Bacteriologic examination was repeatedly negative for tubercle bacilli Bacillus proteus was recovered twice, also diphtheroids and a few hemolytic streptococci The Kolmer and Kline reactions of the blood for syphilis were negative In the intravenous congo red test, 80 per cent of the dye was recovered in 1 hour The reaction to the Frei test was negative The result of the tuberculin test, employing 0 00002 mg of purified protein derivative, was 2 plus A roentgenogram of the chest showed healed shadows in the upper lobe of the right lung but no activity A roentgenogram of the sacrum and lumbar part of the spine made on July 31, 1946, showed superficial bone destruction of the first sacral segment There were no other abnormalties

DISCUSSION

DR REUBEN FRIEDMAN I do not believe that too much significance need be given to the positive tuberculin reaction nor to the fact that the roentgenogram showed shadows in the upper part of the chest Considerable significance should be given to the localization of the lesions and their multiplicity, the numerous sinuses, the purulent character of the discharge, the chronicity and unresponsiveness to treatment and the failure to find tubercle bacilli in the discharges In the circumstances, I suggest a diagnosis of hidradenitis suppurativa

DR JOHN H STOKES It does not necessarily follow that, because a man has tuberculous lesions elsewhere or a positive tuberculin reaction, this has to be tubercuolus One sees in certain young persons a most resistant canalizing pyogenic folliculitis of the buttocks which lasts for years, scarring the whole buttock, and the only thing I know of that it responds to is intramuscular injections of a turpentine solution in olive oil That is on the principle of the old time Netter's abscess treatment for chronic infection—the provocation of a violent reaction in the deep muscle tissue by the use of an agent like turpentine I have treated 1 or 2 patients in that way, and it works well, though it is a long-drawn-out affair Then the manganese salts are useful in some of these patients, given intramuscularly, also over a considerable period of time Potassium permanganate sitz baths produce a striking change One ought to use the proctoscope, to rule out a tuberculous bowel, fistula in ano and so forth Roentgen ray therapy was not conspicuously successful, in my experience Adequate high voltage roentgen ray therapy, however, might help

DR M H SAMITZ I would suggest that a culture be made If penicillin is useless, tyrothricin in one of the new penetrating vehicles might be efficacious

DR HERBERT J SMITH I think that it is hidradenitis suppurativa

DR CARMEN C THOMAS The organisms which were found were tested for streptomycin and penicillin resistance and were found to be sensitive to both I chose penicillin because it is more readily available A proctoscopic examination gave no information I might say that the lesions begin deep in the tissues

sensitive to streptococci She has had two pyogenic flare ups which developed from the food allergy flare ups The first cleared rapidly with local penicillin therapy, and tonight she seems to have something in addition I believe that a sensitivity to penicillin has developed

DR DONALD M PILLSBURY This is in line with Gardner Hopkins' observation that 25 per cent of patients with chronic eczematous eruptions will experience a sensitivity to penicillin

DR JAMES M FLOOD In our patient, reactions to foods occur in about eight hours, vesicles appear in about twelve hours Reactions are practically always evident within twenty-four hours

DR JOHN H STOKES In developing the so-called basal nonallergic diet type of procedure, we started out to determine what the patient is sensitive to, and, incidentally, to find out what he is not sensitive to We began with the so-called allergic diary and in that way picked out pears in our first case as an allergen Then we used the Rowe type of diet in an effort to put the patient on a type of diet which rarely causes allergic response We very soon gave it up Now we use what we call the B-N-A diet (Basal Nonallergic diet) With this procedure it is possible to find out what foods cause flare ups and to put the patient on a diet which does not cause them It is to be pursued unaltered for at least six months after the work-up is completed Many patients are apparently allergic to milk, so that we no longer start with milk after cleaning the intestinal tract with castor oil The patient, after six or seven weeks, is equipped with a simple diet of meats, cereals, starches, vegetables and fruits which have not excited any lesions, and on that diet he lives for not less than six months Thus, by maintaining him on a diet to which he has been experimentally proved not to be reactive, he is desensitized to a wide variety of other foods with which he has not even been tested and finally resumes something approximating a normal diet I think that this procedure ought to be more widely used than it is The patient can develop the diet for himself

Lymphocytoma Cutis Presented by DR JOHN W LENTZ and DR HERMAN BEERMAN

E K, a white man aged 27 years, presents a patchy lichenified coalescent brown-yellow papular dermatosis of the abdominal wall Many papules have seemingly collected about hair follicles The condition began asymptomatically about ten years ago, with pruritus the only symptom, the condition is more pronounced when perspiration is excessive The biopsy specimen showed lymphocytoma cutis (foci of lymphocytes in reticulum, occasional giant cell, parafollicular distribution)

DISCUSSION

DR FRED D WEIDMAN This is another illustration of what I said before about the picture's not fitting precisely into any of the recognized dermatologic patterns

DR JOHN H STOKES I was struck by the possibility of lichen nitidus due to vitamin A deficiency

DR DONALD M PILLSBURY Lichen nitidus was the first on our list of clinical diagnoses

Erythema Nodosum with Rheumatic Fever Presented by DR A T GIORDANO (by invitation) and DR JOHN F WILSON

dispute that has been going on as to whether this is a bullous form of Darier's disease The Baltimore school, for example, adheres to the Darier thesis, and I think that those who saw the sections will agree that in this case, as in the other cases, there is not any feature of importance with respect to hyperkeratosis In my judgment, whatever Hailey and Hailey's concept may turn out to be, it will not be Darier's disease

DR DONALD M PILLSBURY Do you think it a virus infection?

DR FRED D WEIDMAN I think so in the same sense that some think pemphigus a virus disease

DR DONALD M PILLSBURY Do you believe that on the basis of histologic changes dermatitis herpetiformis can be ruled out?

DR FRED D WEIDMAN In this patient, yes There are distinctive lacunas in this disease comparable to those which appear in Darier's disease and which do not appear in dermatitis herpetiformis

DR DONALD M PILLSBURY There is an interesting history The patient felt that the lesions tended to appear just before her menses There seemed to be a menstrual element in the eruption, whatever its nature I think that it would be interesting to follow her and possibly treat her on that basis I have recently followed a patient with an eruption very much like this, but was never able to satisfy myself as to the exact diagnosis She showed fairly good improvement following injections of smallpox vaccine

DR WILBERT SACHS, New York (by invitation) I agree with Dr Weidman that the pathologic picture here is characteristic of the disease and that it is not a type of Darier's disease It seems to me that the type of dyskeratosis found in Darier's disease does permit the formation of bullous lesions I cannot agree with the name familial benign pemphigus of Hailey and Hailey, as I feel that it is a form of epidermolysis bullosa After the lesions disappear, a neurodermatitic type of eruption is left but in these areas, microscopically, one finds lacunas just above the basal cell margin, though these are not clinically manifest

DR HERMAN BEERMAN How would Dr Sachs distinguish this from Darier's disease histologically?

DR WILBERT SACHS, New York (by invitation) In this disease the cells are not dyskeratotic They are larger than normal, the nuclei are well formed and well stained, and corps ronds are absent Also, I have demonstrated in my article mitotic figures in the nuclei, and one never finds mitotic figures in benign, accelerated dyskeratosis

A Case for Diagnosis (Lichen Planus?) Presented by DR G M KNOLL for DR FRANK C KNOWLES

Pemphigus Vulgaris (Early or Benign?) Presented by DR SIGMUND S GREENBAUM

Purpuric Pigmented Lichenoid Dermatitis of Gougerot and Blum Presented by DR D M SIDLICK

Chloracne Presented by DR EDWARD F CORSON

Herpes Gestationis (Erythema Multiforme?) Presented by DR JOHN T WILSON

Morphea Type Scleroderma (Dermatomyositis?) Presented by DR FRANK C KNOWLES and (by invitation) DR H A LUSCOMBE

reactions do not fit the diagnosis of hydroa puerorum One of the reasons I asked the patient to come is that the eruption lacks many of the characteristics of urticaria pigmentosa The lesions apparently do give rise to scarring I thought it a case of urticaria with pigmentation That is just a shift in terminology, and there are no histologic changes to bear this out I am not prepared to make a definite diagnosis

DR STEPHEN T WHELAN (by invitation) The child had dermographism limited to the areas of pigmentation The normal skin has never exhibited any dermographism

Localized Amyloidosis Cutis of the Legs Presented by DR LESLIE NICHOLAS

Keratosis Palmaris et Plantaris (Acquired) Presented by DR H E TWINING

Paget's Disease of the Breast Presented by DR JOHN W LENTZ, DR MEYER L NIEDELMAN and (by invitation) DR GERLACH MAHONEY

Chronic Cheilitis of Undetermined Origin, Photosensitivity Presented by DR DONALD M PILLSBURY

Arsenical Dermatitis Successfully Treated with BAL Presented by DR CARMEN C THOMAS

Pityriasis Rubra Pilaris Presented by DR H E TWINING

Leiomyoma Cutis (Zosteriform) Presented by DR W N NEW, United States Navy, United States Naval Hospital, Philadelphia (by invitation)

F J P, a white man aged 25 years, well developed, well nourished and in apparently good health, presents on the back and right loin a wedge-shaped group of discrets papules and nodules, slightly reddened, nodular and intradermal in the region of the cutaneous distribution of the tenth thoracic nerve The nodules are firm, slightly tender and not fixed to underlying structures and vary in size from 2 mm to 10 mm Some give the appearance of following the lines of cleavage in a linear fashion Lesions are present on the right side of the face and the right side of the neck, reaching up to the hair line They are discrete and slightly reddened and appear more transparent than the lesions on the back They vary in size up to 8 mm Approximately ten years ago the patient noticed papules on the right side of the back and face He has noticed a burning sensation of the lesions on the back during the past two years, especially when emotionally upset The results of laboratory tests are essentially negative

In the lower part of the dermis there were groups and strands of smooth muscle One of them was a longitudinal section which was adjacent to a hair follicle and might represent hypertrophy of the levator muscle adjacent to this hair follicle In other areas, smooth muscle fibers were seen in cross section Histologically, this specimen indicated a leiomyoma The patient has been seen by plastic surgeons, who advised that the lesions were too widespread for surgical removal

folliculitis decalvans, described by Quinquaud He insists that pseudopelade is never associated with folliculitis and that it occurs in the form of discrete patches which perhaps may coalesce, as they did in this case, whereas folliculitis decalvans is characterized by uniform folliculitis Later, in the cicatricial alopecia, they may not be differentiated one from the other, but in the earlier stages they are definitely different

DR SIGMUND S GREENBAUM Pelade is the French term for alopecia areata The term pseudopelade would therefore indicate the absence of clinically apparent folliculitis Pseudopelade is, apparently, a noninflammatory, slowly progressive cicatricial alopecia

DR LOUIS GOLDSTEIN Since he was exposed to the sun, it is possible that the patient had lupus erythematosus, which has subsided, especially since he had crusting on the scalp

DR SIGMUND S GREENBAUM In lupus erythematosus the lesions usually are circinate in outline, Brocq established the point that in pseudopelade the lesions show a peculiar irregularity, a shooting out of the lesions into the surrounding skin The glassy sheath, furthermore, is pathognomonic of pseudopelade so I think the diagnosis is inescapable Pustulation is essential to folliculitis decalvans, and there certainly is no pustulation here, and the patient gives no history of a previous pyogenic eruption

Acne Necrotica Miliaris Presented by DR REUBEN FRIEDMAN and (by invitation) DR CONRAD STRITZLER

R E, a white man aged 42 years, when first examined in October 1945, showed the scalp studded with hundreds of pinhead to match head-sized, reddish brown papules with crusted, necrotic, depressed summits Many appeared in the hairline and many in the bearded region, and there were about thirty lesions in the interscapular region Some had undergone involution, leaving depressed, crateriform, pinhead to match head-sized scars A few centrally depressed papules were present on the nasal half of each orbital ridge, and one was noted on the left nasolabial fold The dermatitis began in 1943 with small, itchy lesions of the scalp which slowly increased in number by the addition of small crops In 1945 similar lesions appeared on the face and back

Treatment included subfractional doses of roentgen ray, staphylococcus toxoid once weekly for ten weeks, tyrothricin ointment, and penicillin ointment, 500 units a gram in water-miscible base There was no improvement The patient improved considerably when given 100,000 units of penicillin in cholesterolized peanut oil daily for six days

Staphylococcus aureus, nonhemolytic and coagulase positive, was found on culture Dr Fred D Weidman's pathologic diagnosis was resolving folliculitis or acne varioliformis

DISCUSSION

DR CARROLL S WRIGHT I wish to mention a simple treatment that Dr Schamberg used to employe—a 1 600 dilution of bichloride of mercury in 70 per cent alcohol I have seen these cases respond miraculously to this treatment It might be worth trying in this case although I admit that the condition is more severe and widespread than any other of this type that I have ever seen

DR HERMAN BEERMAN Could this be a follicular seborrheic dermatitis

DR SIGMUND S GREENBAUM I wish to take exception to the term "miliaris" as applied to this case since that term is generally applied to the presence of but

mycotic and seborrheic conditions of the skin) and ultraviolet rays, with only slight improvement He has also received roentgen therapy, a total of 100 r through a 1 mm aluminum filter

DISCUSSION

DR MORRIS MARKOWITZ I think that the disease is lichen simplex of Vidal of the hypertrophic type It has the crisscross markings

DR M H SAMITZ This man said that the dermatosis began as a small patch which he scratched and the present condition developed from that I think that it is lichen simplex of Vidal

DR FRED D WEIDMAN I think that we can exclude the diagnosis of lichen simplex of Vidal There is an extremely dense infiltration of cells, something that one never sees in lichen simplex of Vidal Maybe it is premycotic mycosis fungoides, but that is difficult to diagnose in any circumstances

DR HERMAN BEERMAN I understand that this is gigantic lichenification I call attention again to the articles of Ronchese (Neurodermatitis with Giant Lichenification, ARCH DERMAT & SYPH **43** 920, 1941), and Berlin (Lichenificatio Gigantea, ARCH DERMAT & SYPH **30**.1012 [June] 1939) in this connection

DR VAUGHN C GARNER One thing appears to me to contradict the diagnosis of lichen simplex of Vidal, namely, the sharp circumscription of this lesion with an indurated border In lichenifications there is a confluence at the center but toward the border the lichenification becomes sparse and more or less discrete It impressed me clinically as being some type of granuloma The thick corded sharply circumscribed border is difficult to reconcile with a diagnosis of simple lichenification

DR CARMEN C THOMAS There has been considerable difference of opinion as to diagnosis on the part of the various pathologists who have studied the sections Some favored lichen planus, a diagnosis which does not conform to the clinical picture, and others a diagnosis of lymphoblastoma This would be most unusual in a 17 year old lesion limited to one site Although in the beginning the lesion may have been pruritic, the patient now complains of little itching and does not scratch frequently I do not believe that it can be the result of scratching

DR REUBEN FRIEDMAN I suggest application of solid carbon dioxide

DR MORRIS MARKOWITZ Pure coal tar applied every day, painted one coat on top of the other, would produce desquamation with improvement

Tuberculous (?) Infection of the Buttocks and Perianal Region Presented by DR CARMEN C THOMAS

R G, a white man aged 35 years, has both buttocks perforated by numerous sinuses which discharge a gray-yellow, thin pus with a fecal odor On the left side of the ischium a recent, as yet unperforated, lesion which is tender, but not hot, is forming Many sinus tracts are open about the perineum, where there is considerable epithelial hypertrophy and the skin is thrown into folds with papillary projections There is no encroachment palpable on the rectal lumen There is bilateral inguinal adenopathy In 1940 a small perianal (ischiorectal?) abscess was drained surgically, and, shortly after, a number of draining sinuses developed around the anus, later involving the buttocks and perineum and requiring a number of surgical drainages, although many perforate spontaneously There has been a loss of 20 pounds (9 Kg) in weight in six months

plasma cells mostly, which obscured the basement membrane There was no evidence of malignancy The diagnosis was some form of focal chronic inflammation of the palate

Cicatrizing Epithelioma of the Scalp Presented by DR SIGMUND S GREENBAUM

Scleroderma Presented by DR E R GROSS and DR CARROLL S WRIGHT

M A, a white woman aged 67 years, presents a silver dollar-sized, hard circumscribed lesion on the left side of the chest The dorsum of both hands and forearms is thickened and boardlike There is similar involvement of the extensor surfaces of both legs, with superficial ulceration of the left leg The disease began with stiffness of all joints, and the backs of the hands became "hardened" These changes spread gradually to the forearms and legs

The patient has received bismuth sodium triglycollamate (bistrimate®), 225 mg daily, since July 23, 1946, with great improvement She says that the sensation of tightness is gone and the skin feels softer and warmer

J M Schildkraut, M D, *Chairman*

Douglass A Decker, M D, *Secretary*

Feb 21, 1947

Dermatitis Herpetiformis in a Woman Aged 72 Years Presented by DR M H SAMITZ and (by invitation) DR P N HORVATH

Lupus Erythematosus with Superimposed Epithelioma? Presented by DR C S LIVINGOOD and (by invitation) DR K KATZENSTEIN

Lipophagic Granuloma at Sites of Intramuscular Injections Presented by DR C S LIVINGOOD and (by invitation) DR W B SHELLEY

Chromoblastomycosis (Recurrence in Case Reported in The Archives 43 62 [Jan] 1941) Presented by DR DONALD M PILLSBURY AND DR IRA L SCHAMBERG

Ichthyosis Hystrix Presented by DR DONALD M PILLSBURY, DR C S LIVINGOOD and (by invitation) DR J P SCULLY

J P, a white boy aged 2 years, alert and well nourished, presents keratinous, spinous-like processes involving the knees, elbows, forearms, wrists and the lateral surfaces of the neck Studies of sweating indicate that only the skin of the forehead has normally functioning sweat glands and that temperature control is relatively poor The maternal grandmother had ten children, five male and five female Four male children died at or soon after birth, of unknown cause A maternal aunt has had three pregnancies, with death at birth of the infants, all of whom were male This patient is the result of his mother's only pregnancy There was normal, full term, spontaneous delivery The birth weight of the patient was 7 pounds 9 ounces (3,430 Gm) When the mother first observed her infant on the third postpartum day, she noted what she described as "large, clear, fluid-filled blisters" on the infant's face and body, with the exception of the palms and soles These vesicles recurred during the first year and a half of life, but with less and less frequency When the baby was 6 months old, the mother noted

and are then not at all red They gradually work to the surface and eventually perforate I think that there must be a deep focus, which is against the diagnosis of hidradenitis suppurativa

Severe Pyogenic Sycosis of the Beard (Lymphedema? Submental Reigon) Presented by DR CARMEN C THOMAS

Noduloulcerative Syphilide of the Body, Gumma of the Scalp (Radiodermatitis with Ulcer?) Presented by DR CARMEN C THOMAS

Widespread Lupus Erythematosus with Depigmentation in a Negro? (Lichen Planus?) Presented by DR CARMEN C THOMAS

J M Schildkraut, M D, *Chairman*

Douglass A Decker, M D, *Secretary*

Nov 15, 1946

A Case for Diagnosis (Necrobiosis Lipoidica Without Hyperglycemia?) Presented by DR EDWARD F CORSON

Pityriasis Rubra Pilaris Improved by Treatment with Vitamin A Presented by DR KNOLL for DR FRANK C KNOWLES

Familial Benign Chronic Pemphigus (Hailey and Hailey Disease) Presented by DR ARTHUR G PRATT

M S, a white woman aged 35 years, first had blisters on the sides of her neck five years ago After several months, the rash healed, leaving residual pigmentation This has recurred constantly and the patient has been free of the rash only about two months at any time during the past five years At the height of an attack, an area approximately 10 by 7 cm at each side of the neck is covered with an oozing, crusted patch of vesiculation and pustulation During the interval of healing, the areas show only residual grayish pigmentation In each axilla there is mild seborrheic dermatitis

The patient's father and her paternal grandmother have had a chronic rash of unknown type in the axillas for years Her five brothers and one sister are normal The medical examination resulted in normal observations The result of the Mazzini test for syphilis was negative The blood cell count was normal except for 7 per cent eosinophils

The report on the biopsy specimen showed slight hyperplasia of the rete cells with decided acantholysis Numerous leukocytes were found on the surface of the epidermis as well as in the corium There was moderate downward extension of the rete pegs and considerable edema of the corium, especially in the papillary portion, with vascular dilatation

The patient was given 1 5 Gm of sulfapyridine daily for seven days, with complete healing of the lesion except for pigmentation Boric acid ointment was used locally

DISCUSSION

DR FRED D WEIDMAN I agree with the diagnosis because I saw the section, but tonight it is not clinically distinctive The histologic picture is distinctive except that in this particular lesion there is more suppuration than usual, that, of course, could very well be secondary infection Most of us are aware of the

Book Reviews

Common Skin Diseases By A C Roxburgh, M D Eighth edition Price, $7 Pp 497, with 220 illustrations Philadelphia The Blakiston Company, 1948

This book was written for a general practitioners' series It is well and generously illustrated The photographs are excellent, and the subject matter is presented clearly and simply This last-mentioned attribute necessitates some sacrifice of well rounded opinion, one result being the inclusion of lichen sclerosus et atrophicus as an atrophic form of lichen planus without any comment Also, the distinctive burning character of the itching in dermatitis herpetiformis is not mentioned

Because the book was revised in 1947 or earlier, there is no mention of fatty acids in accounts of the treatment of superficial fungous infections The only mention of antihistaminic drugs is a single line footnote on diphenhydramine hydrochloride (benadryl®) Streptomycin is not mentioned with reference to the treatment of granuloma inguinale or tuberculosis cutis The treatment of syphilis is not discussed, but the reader is referred to texts on venereal diseases for "the mapharsen and bismuth therapy" without mention of penicillin

The treatment presented is carefully discussed However, considering that the book was designed for general practitioners, Whitfield's ointment is overemphasized for the treatment of superficial fungous infections at the expense of blander and less risky measures Penicillin ointment is recommended for eczema and infectious eczematoid dermatitis, two conditions in treatment of which it may sensitize most easily

This book is very useful for the instruction of general practitioners As noted previously, treatment mentioned is not as up-to-date as the book's year of publication in this country might indicate, and the work was not received for review until March 1949

CORRECTION

In the article by Drs Curtis and Cawley, in the August issue of the ARCHIVES, the first sentence of the last paragraph on page 140 should read "In addition to the training already received Dr Wile accepted on his return to New York a position with Sigmund Pollitzer as instructor in dermatology and syphilology at the Post-Graduate Medical School and Hospital and as his assistant at the Lenox Hill Hospital"

J M Schildkraut, M D, *Chairman*

Douglass A Decker, M D, *Secretary*

Jan 17, 1947

A Case for Diagnosis (Barraquer-Ferre Lipodystrophy?) Presented by Dr Reuben Friedman and (by invitation) Dr Conrad Stritzler

About seven years ago a group of brownish patches developed above the right knee in a white woman aged 37 years There was no swelling, pain or fever This progressed slowly until at present the inner aspect of the right thigh from the internal condyle to the junction of the middle and upper thirds presents an irregular oval area of greenish yellow discoloration which is atrophic and depressed below the level of the surrounding normal skin It is 22 cm in its long diameter and 9 cm in width The margin fades into the surrounding normal skin The skin is harsh, roughened and atrophic, and a few telangiectatic vessels are noted There is diminution in the subcutaneous fat The skin is freely movable, and there is no associated pain or tenderness The neurologic examination, an air myelogram and roentgenograms of the spine revealed no abnormalities The blood count, urinalysis and serologic tests of the blood for syphilis gave negative results

The histologic section showed atrophy of the epidermis There were no inflammatory changes in the corium or subcutaneous tissue Sweat glands and sebaceous glands were preserved

DISCUSSION

Dr Morris Markowitz The cholesterol and ester contents are normal, and in lipodystrophy one would expect some disturbance in the cholesterol content

Dr Reuben Friedman There is also an associated muscular disturbance involving the interosseous spaces on the same side, and there is slight atrophy in the left hand The process is one of muscular atrophy

Dr Sigmund S Greenbaum I think this is a case of panniculitis of the nonfebrile type There is atrophy of the adipose tissue, but I could not see any muscle atrophy as she stretched both legs for comparison

Dr Reuben Friedman The patient has never had any nodules, pain or fever Sections failed to reveal signs of panniculitis or inflammation

Pseudopelade (Folliculitis Decalvans?) Presented by Dr Reuben Friedman and (by invitation) Dr Conrad Stritzler

B M, a white man aged 28 years, well nourished and well developed, presents an irregular band of alopecia stretching across the middle of the scalp just anterior to the vertex The follicular orifices are prominent in the periphery of the patch, which is pink and atrophic throughout A few normal hairs appear here and there throughout the patch Extracted hairs show a glassy sheath about the roots The patient spent two and a half years in the desert of south Iran while in the service from 1943 to 1945 During this period the scalp became dry and scaly Several weeks after his return home, in December 1945, "scabs" developed on the scalp He was treated with shampoos, ointments and lotions In July 1946 the "scabs" fell off, and none appeared thereafter

Tyrothricin has been applied locally The lesion has *not progressed since* institution of this therapy

Dr Reuben Friedman Sutton's book on dermatology considers pseudopelade and folliculitis decalvans as synonymous, while McCarthy goes to considerable trouble to point out that Brocq, who described pseudopelade, differentiated it from

a few minute lesions scattered throughout the scalp associated with itching Often one will see it in women or men who complain only of itching, and then on examination one finds a minute lesion around the hair as it emerges from the follicle This man has major acne necrotica, and, as Dr Wright states, it is a simple matter to clear up with either bichloride of mercury or with sulphur, but, as in tinea versicolor and seborrheic dermatitis, treatment must be continued for a long time to prevent recurrences

DR REUBEN FRIEDMAN Dr Stritzler adds that we did use a 1 1,000 dilution of bichloride of mercury in 70 per cent alcohol but discontinued its use because it was ineffective

DR VAUGHN C GARNER Montgomery, of the Mayo Clinic, has written extensively on this subject These lesions certainly are not miliary, and while it definitely conforms to the diagnosis of acne necrotica, I think it differs from the acne miliaris in the Mongomery sense Montgomery advocates the use of ammoniated mercury in the cases in which the scalp is affected, and several patients whom I have seen have done extremely well under that regimen

DR SIGMUND S GREENBAUM The best experimental work on acne necrotica was carried on by Dr Weidman and Dr Strumia some years ago, in which they demonstrated an organismal cause for acne necrotica (Experimental Acne Varioliformis, Arch Derm & Syph **10** 702-713, 1924)

Kaposi's Idiopathic Pigmented Sarcoma? Chromoblastomycosis? Presented by DR REUBEN FRIEDMAN and (by invitation) DR CONRAD STRITZLER

A Case for Diagnosis (Erythroplasia?) Presented by DR SIGMUND S GREENBAUM

A T, a white man aged 31 years, has three fourths of the palate involved with a deep red, well defined patch which has a smooth periphery and a central portion showing irregular elevations which are soft to the touch (almost velvety) Just in front of the soft palate, at the center, there is a slightly infiltrated area At first it was recurrent, but since 1943 it has been a persistent lesion The patient first noticed a tender papule in the center of the palate This was treated with local applications, but the lesion gradually became larger In July 1944 new dentures were prescribed, and profuse bleeding occurred for twenty-one days after they were worn for two days Dentures of the "roofless" type were prescribed in June 1945, and within forty-eight hours inflammation, swelling, tenderness and bleeding increased New dentures of a metallic material (tantalum?) were prescribed in October 1945, which caused an exaggeration of symptoms At present the patient uses dentures only when eating and during business appointments, approximately two hours a day The lesion is apparently at a standstill The patient had streptococcic septicemia on three occasions eight to twelve years ago, while working as a butcher His mother died at the age of 55 of carcinoma and his father at the age of 59 from an unknown cause Two brothers and four sisters are all living and well

Routine laboratory tests resulted in findings that were within normal limits the Kahn reaction of the blood was negative A biopsy specimen examined in August at the Naval Hospital in Fort Eustis, Virginia, was reported as chronic inflammatory tissue

The follow-up report of the second biopsy stated that the specimen included the mucosa and a bit of submucosa The epithelium of the mucosa was moderately thickened and extended downward in long rete pegs The cells were not atypical In the corium there was a dense chronic inflammatory exudate of lymphocytes and

Hospitals of the American Medical Association as qualified to teach graduate students for periods of from one to three years The American Board of Dermatology and Syphilology has now certified 1,001 candidates in the United States, Canada and Cuba If present trends continue, the already large number of experts will increase even more rapidly during the next few years

An examination of the record shows that 40 per cent of the present chiefs of service in the 80 approved institutions received their training —and with it the inspiration to become leaders in their field—from four men, namely, Dr George M MacKee, Dr Udo J Wile, Dr John H Stokes and Dr Harold N Cole Without disparagement of the attainments of others in this respect, these four men may be said to have affected profoundly the progress of the specialty in this country

SURVEY OF APPROVED INSTITUTIONS

Of the 80 institutions now approved for graduate training in dermatology and syphilology, 31 are approved for the full three year training, 26 are approved for two year residencies, 15 are approved for one year training and 4 others have emergency approval for one year Three institutions are approved for one year of training in syphilis and 1 for one year of training in pathology One year of postgraduate instruction is given in 4 institutions With the exception of a school year of basic science in a few medical schools, the Board has not recognized postgraduate training for fractional periods of a year

For the most part, the program in these approved institutions emphasizes informal teaching, with stress on supervised case study, laboratory work and informal conferences Fundamental research by students in training is seldom possible, except in three year institutions with small enrolment or in places where there exists a close rapport with basic science departments of medical schools Formal, didactic courses have been given impetus in recent years because of the large number of candidates from the Services An analysis of the records shows that this type of instruction is inferior to the more personal informal training which stimulates the initiative and individual ability of the student Close, personal supervision of the student in training by either the chief of staff or well trained associates is a necessity for the best results Needless to say the chief is responsible not only for the development of superior clinical dermatologists but also for the encouragement of constructive and independent thinking

In an analysis of 10 three year institutions having the largest number of applicants for the Board certificate the average marks of the candidates from the separate institutions were seen to vary from 83 7 to 77 8 It did not appear that a person having a high grade was necessarily superior with respect to future leadership and scientific attain-

a tendency of the skin on the elbows, knees, legs and arms to become dry and scaling, then the development of thick keratinous spines as now seen

The child has been previously given thyroid, "1 tablet three times daily," over a six months' period, without benefit Breast feeding was discontinued at 3 months, and various other dietary changes were of no benefit Locally applied ointments were ineffectual

The dentition, hair and nails are normal The general health and mental development are excellent There are no abnormalities except in the skin

The complete blood cell count was within normal limits The fasting blood sugar, blood phosphorus and serum cholesterol were within normal limits The results of serologic tests of the blood for syphilis were negative The roentgenogram of the chest was normal The eyes were normal The diagnosis from biopsy was ichthyosis, hyperkeratosis, acanthosis and vacuolization of the epidermis

DISCUSSION

DR JOHN P SCULLY (by invitation) Does anyone think that high doses of vitamin A might be of some benefit in this case? Could we seriously consider the possibility of these male infant deaths in the family as being due to a dermatologic condition such as this or at least a hipogene in the family tree of which this may be a variant, which would induce us to advise the female members of the family to avoid conception?

DR MORRIS MARKOWITZ Ichthyosis hystrix has been treated with sodium chloride baths or ointments with improvement in the condition

DR M H SAMITZ To grease a dry skin, one should use either animal or vegetable fat Greases from the petroleum family will only degrease the skin I advise the use of wool fat rather than aquaphor® (an oxycholesterol-petrolatum ointment base)

DR H H PERLMAN I have tried vitamin A in ichthyosis without improvement I have ceased making vitamin A determinations because the vitamin A content of the vascular system is not necessarily an index of the vitamin A content of the liver

LIEUTENANT FITZPATRICK (by invitation) When this disease is present at birth, it will probably not respond to the administration of vitamin A Keratotic diseases that develop during life will respond to the administration of vitamin A

CAPTAIN R L GILMAN In view of the family history, it would be interesting to get the Rh factors in this boy's parents I agree with the presenters that this is something more than ichthyosis

DR C S LIVINGOOD We had a patient whom we followed closely with controlled areas treated with sodium chloride ointments versus other types of greases, without any significant difference

DR MORRIS MARKOWITZ I have tried sodium chloride therapy in keratosis palmaris et plantaris with considerable success I have not tried it in ichthyosis

Keratoderma Palmaris et Plantaris (Improvement with Vitamin A Therapy Presented by DR H H PERLMAN

Onychomycosis Presented by DR D M PILLSBURY, DR C S LIVINGOOD and (by invitation) DR J P SCULLY

by part time work in clinics over a period of years Most of the chiefs who had been in general practice were admitted as founders, for the 7 who took the examination, the average mark (80 4) was below the average for all the chiefs who were so tested

Fourteen of the chiefs had received some foreign training, for 4 the training had been exclusively foreign In some instances the available data did not include the specific length of training, but it was estimated that the average length of instruction was two years and two months Some 70 per cent had received their training in a single institution Over 50 per cent had been trained in one of 7 leading institutions While the longer the training, the better the prospect of prominence in the field, several chiefs of service who had had short terms of formal training are notable exceptions Seniority, sole availability and opportunism may have been responsible for some of the appointments, but most have been due to superior ability and initiative It is significant that only 8 per cent of the 63 are engaged in full time work in hospitals and universities The remainder are part time practitioners, with a considerable variation in the amount of time spent in the institutions In general it would seem that success in training men does not depend merely on constant attendance but rather is due to a combination of high ideals, superior intelligence ability to inspire students and insistence on continued effort and development

EVALUATION OF CANDIDATES

There has been some criticism of the Board because students are said to study with the sole object of passing the examinations It would appear that this criticism is not justified It is no doubt true that many students are of such mental stature that the desire to become proficient would serve as a sufficient incentive It is also indisputable that many graduate students lack initiative and, unless there is a definite objective, such as the examinations, will not work as assiduously as otherwise It is our belief that pointing for the examinations has a salutary effect on the average candidate and results in an increased factual knowledge of the specialty It must be considered the responsibility of the chief of service to teach students to think Students are later expected to meet minimal standards of competence in the theoretic and practical aspects of the specialty, but preparing for the examinations should not interfere with their development

A comparison of A candidates (those in the specialty for ten years) with the B group (persons with three years of training) revealed little or no difference in the performance provided that the same age levels were compared However, a candidate over the age of 46 had an average mark of 78 3, while B candidates 35 years of age or younger had an average mark of 83 2 The rate of failure was slightly higher in the older age A group (table 2)

Editorial Note

At last the issues of the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY are current Differences with the printers' union and inability to obtain sufficient editorial help have made the past year difficult

Miss Jewel Whelan, who was complimented at the last convention for her many years of service to the Association, has found it necessary to withdraw from the position of Assistant to the Managing Editor Her unstinted efforts and the valuable part she played in the preparation of the ARCHIVES are greatly appreciated Dr Richard J Plunkett will now be in charge of the production of the ARCHIVES, having recently been made Managing Editor of Special Publications of the American Medical Association

The present plan is to resume the publication of abstracts of dermatologic meetings in the near future It is hoped that a supplementary issue limited to transactions may be published this fall The use of color in photomicrographs and in other illustrations is not as yet possible except on rare occasions, because of the prohibitive cost

Our thanks are expressed to our readers, who have tolerated the delay in the appearance of the ARCHIVES during the past months, and to our contributors, who have waited months for the publication of their articles with only an occasional objection

THE EDITORIAL BOARD

DISTRIBUTION OF CERTIFIED SPECIALISTS

The number and concentration of certified dermatologists in the larger cities of the United States is shown in table 5 It would appear that Washington, D C, is in greatest supply However, a fair analysis is difficult, as many of the cities have had nothing short of phenomenal increases in population since 1940, the date of the last census Consequently the per capita distribution shown may be grossly in error It

TABLE 5.—*Distribution of Certified Specialists, by Cities, in December 1947*

City	Number of Certified Specialists	Population (1940)	Per Capita Distribution
New York	195	7,454,995	1 38,062
Chicago	50	3,396,808	1 67,936
Philadelphia	35	1,931,334	1 55,238
Washington, D C	31	663,091	1 21,370
Los Angeles	28	1 504 277	1 53 709
Boston	22	770,816	1 35 037
Cleveland	20	878,336	1 43,916
San Francisco	19	634 536	1 33 396
Detroit	17	1 62 ,452	1 95,497
Pittsburgh	15	671 659	1 51 310
St Louis	14	816 048	1 58 289
Baltimore	12	859 100	1 71,591
New Orleans	11	494 537	1 44,957
Cincinnati	9	455 610	1 50 62
Denver	9	322 412	1 35,823
Milwaukee	9	587 472	1 65,274
Minneapolis	8	492,370	1 61 546
Newark, N J	8	429,760	1 53,720
Portland Ore	8	305 394	1 38 174
Buffalo	7	575,901	1 82 271
Dallas, Texas	7	294,734	1 42 104
Kansas City Mo	7	399,178	1 57,025
Oakland, Calif	7	302,16	1 4 169
Atlanta Ga	6	302,288	1 50,381
Birmingham Ala	6	267,358	1 44 597
Houston, Texas	6	384,514	1 64,085
Oklahoma City	6	204,424	1 34,070
San Diego Calif	6	203,341	1 33 890
Indianapolis	5	386 972	1 77 394
Richmond Va	5	193 042	1 38,605
San Antonio Texas	5	253,854	1 50,770
Total	589	28 059 991	1 47 640

is obvious however that there is a disproportion in the number of certified dermatologists per capita in various cities Specifically New York has twice as many dermatologists per capita as has Chicago, which, in turn is proportionately much more heavily supplied with specialists than are many other large cities It is clear that the saturation point is near in some centers and equally clear that several other cities may yet support additional dermatosyphilologists It is of further interest that the 589 dermatologists in these thirty-one cities comprise

Archives of Dermatology and Syphilology

VOLUME 60 OCTOBER 1949 NUMBER 4

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PRESENT STATUS OF DERMATOLOGIC TRAINING IN THE UNITED STATES

FRANCIS E SENEAR, M D
CHICAGO
AND
GEORGE M LEWIS, M D
AND
FRANK E CORMIA, M D
NEW YORK

FROM the many signs, it would seem that dermatology is at the crossroads In common with other medical specialties, it has progressed a long way, but it cannot remain static The future must of necessity be one of expansion The time has now arrived when those specializing in this branch of medicine must consider seriously the direction of further growth It would appear logical at this time for them to examine the record of past and present performance in order to help chart an enlightened course for the future Perhaps in this way some of the pitfalls and errors of this and preceding generations may be avoided The records of the American Board of Dermatology and Syphilology have been carefully scrutinized, the opportunities for training, together with the background of the chiefs of service of approved institutions, have been analyzed, the present methods of teaching have been considered, and the performance of certified specialists has been evaluated In addition, the present distribution of certified dermatologists in the United States has been determined On the basis of the inequalities found, recommendations will be made

GROWTH OF MODERN AMERICAN DERMATOLOGY

When the American Board of Dermatology and Syphilology was formed in 1932, there was only a handful of graduate training centers for the teaching of dermatology and syphilology in the United States In 1940, when the first list of approved institutions was published, only 20 institutions were included Today, there are 80 institutions approved jointly by the Board and by the Council on Medical Education and

Read before the Section on Dermatology and Syphilology at the Ninety-Seventh Annual Session of the American Medical Association, Chicago, June 24, 1948

From the Department of Dermatology, Research and Educational Hospitals, University of Illinois College of Medicine, and the Department of Medicine (Dermatology), New York Hospital and Cornell University Medical College

TABLE 6—*Specialists Certified by the American Board of Dermatology and Syphilology as of December 1947, by State and Geographic Divisions*

Section and State	Number of Certified Specialists	State Population (1945)	Per Capita Distribution
New England			
Maine	0	810,415	
New Hampshire	1	467,516	1 467,516
Vermont	0	328,554	
Massachusetts	27	4,185,282	1 155,010
Connecticut	12	1,794,003	1 149 500
Rhode Island	4	733,186	1 183,296
Total	44	8,318,956	1 189 071
Middle Atlantic			
New York	206	12,817,782	1 64 312
Pennsylvania	59	9,299,579	1 157,619
New Jersey	35	3,912,236	1 111,778
Total	330	26,029 597	1 78 877
South Atlantic			
Delaware	4	275,964	1 68,991
Maryland	13	2,014,387	1 154 952
District of Columbia	31	880,044	1 28,388
West Virginia	3	1,694,577	1 563,859
Virginia	11	2,937,282	1 267,025
North Carolina	7	3,514,297	1 502,042
South Carolina	4	1,912,960	1 478,240
Georgia	7	3,041,969	1 434,567
Florida	8	2,313,393	1 289 174
Total	88	18,584,873	1 211,191
East North Central			
Wisconsin	12	2,948,262	1 245,688
Michigan	31	5,589 324	1 148 042
Illinois	61	7,486,225	1 122,726
Indiana	10	3,517,277	1 351 727
Ohio	47	6,858,785	1 145,931
Total	161	26,399,873	1 163,880
East South Central			
Kentucky	4	2,598,393	1 649 598
Tennessee	8	2,822,959	1 352,869
Mississippi	3	2,126,175	1 708,728
Alabama	7	2,710,601	1 387,228
Total	22	10,258,128	1 466,278
West North Central			
Minnesota	18	2,630,157	1 146,119
Iowa	5	2,391,213	1 478,242
Missouri	12	3,554 466	1 296,205
North Dakota	1	517,388	1 517,388
South Dakota	0	544,089	
Nebraska	6	1,229 674	1 204,945
Kansas	2	1,784,474	1 892,237
Total	54	12,651,461	1 234 286
West South Central			
Oklahoma	8	2,124,250	1 265 531
Arkansas	3	1 851,086	1 617,028
Texas	30	6 696,931	1 223 231
Louisiana	11	2,399,772	1 218,161
Total	52	13,072 039	1 251,385
Mountain			
Montana	0	451,793	
Idaho	0	489,164	
Wyoming	0	248,753	
Nevada	1	142 002	1 142 002
Utah	0	600,692	
Colorado	10	1,075 647	1 107 564
Arizona	1	581 586	1 581,586
New Mexico	1	534 248	1 534 248
Total	13	4 123,885	1 317 221
Pacific			
Washington	9	2 162 906	1 240 322
Oregon	8	1 315 676	1 164 459
California	71	9 101 131	1 128 466
Total	88	12 579 713	1 142 610
Total for United States	852	132 018 520	1 155 711

ment, but only that he had amassed a large amount of factual knowledge Superior rating in the examinations did not necessarily indicate the possession of exceptional reasoning ability However, consistently inferior grades in an institution are presumptive evidence of poor selection of candidates, faulty program and/or a lack of inspirational leadership by the chief of staff

Deficiencies in the examination were further investigated by an analysis of the percentage of failures in individual subjects in the various institutions (table 1) As can be readily seen, the teaching of pathology is inadequate in the majority of institutions in the United States There is also apparent a spotty deficiency in the instruction of certain other subjects In a further analysis, the average number of subjects failed by candidates from the various institutions was determined With the exception of 4 hospitals, the subject-failing rate in the

TABLE 1—*Percentages of Failure, by Subjects, of Candidates Trained in 10 Different Institutions*

Institution	Percentage of Failures in One Subject or More	Percentage of Failures, by Subject						
		Clinical Cases	General Dermatology	Syphilis	Pathology	Mycology	Allergy	Physical Therapy
A	53 8	8 0	8 0	8 0	53 8	23 0		23 0
B	41 0	2 5	2 5	18 0	25 3	2 5	5 0	5 0
C	39 0	11 0	6 0	11 0	24 0	6 0	2 5	6 0
D	31 0	2 4		4 8	21 9			9 7
E	28 0	2 3	2 3	7 0	16 2	1 6	2 3	
F	28 0	12 5	9 7	3 1	6 2	3 1		9 7
G	21 0				18 4	2 6		2 6
H	19 5	7 4		2 4	12 0	4 8		4 8
I	19 0	14 3	4 7	4 7	14 3	4 7	4 7	
J	16 6	6 2	6 2	4 1	10 4	8 3	2 0	2 0

institutions approved for three year training averaged between 1 0 and 1 5 for each failing or conditioned candidate In the 4 excepted institutions, the subject-failing rate by this group of candidates was between 2 3 and 2 5, indicating substandard training in several subjects

CHIEFS OF INSTITUTIONS

There are 63 certified specialists of the American Board of Dermatology and Syphilology who are chiefs of service in 77 of the 80 institutions approved for graduate training, the remaining 3 chiefs are not dermatosyphilologists Of the 63, 30 were in the founders' group and 33 took the examinations The average mark of the latter group was 83 6 which was only slightly better than that of the B candidates (aged 25 to 35), 83 2

It is of interest that 25 per cent of the chiefs had a background of general practice averaging 4 4 years, for the most part, their total training was of shorter duration than that of the remainder of the chiefs In some instances, proficiency in the specialty was acquired

take the examination Not infrequently students lack one or two months of the required three years of training and in some instances have remained in training in order to qualify, when they could have accepted a desirable position The capacity of students to absorb information is variable Nevertheless, a minimum of three years of training would appear desirable in almost all cases It would also appear that it would be unwise to permit the candidate to determine for himself the duration of training, though the doing so would save the Board a great deal of work and expense

Selection of students for training is of the greatest importance Perhaps more thought should be given to attracting the better students, rather than waiting for applicants to appear It is a direct responsibility of the chiefs of service to accept students, not because of their ability to meet tuition or for other extraneous reasons, but rather because of their superior record in medical school and internship and for their intrinsic potentialities as determined by personal observation It should be a prime duty of the chief to take a personal interest in the training of his men and later to assist them in finding locations best suited to their individual qualifications As O'Leary emphasized, the superior candidate should have the opportunity on graduation to develop further under supervision Students with exceptional promise should be encouraged to direct their energies toward fundamental research and as potential leaders in dermatology, should be given gradually increasing responsibilities in teaching and in clinic management It is by rigorous selection and equally rigorous training that dermatology will increase its stature as an independent and important medical specialty

ABSTRACT OF DISCUSSION

Dr Marion B Sulzberger, New York We are grateful to the presenters for this most valuable guide to those who are responsible for training men in graduate courses in dermatology and syphilology I think it will become a bible to most of us

I should like to ask whether there is any possibility that something might be added to the Board examinations I am certain that, in the aggregate, the goal of certification by the specialty board is an excellent influence and has assisted and will elevate the standing of the specialty There are many men who would not study hard for three years and would not be properly trained unless the examination and the objective of certification were before them Nevertheless, there is a small but most important group of men who should become teachers and leaders of investigation, who are not training primarily to become practitioners or to pass examinations It would be very desirable if these men were permitted to spend a good part of their three years of training on some selected matters which Drs Senear, Lewis and Cormia have mentioned, such as investigative work and its technics, fundamental studies in basic sciences and in fields related to the specialty, the methods of organization of departments and hospitals and teaching clinics, the pedagogic technics, the statistical technics, the sociologic aspects of cutaneous medicine and the history of cutaneous and general medicine during their period of study

A survey of the subjects failed by 211 candidates [1] is shown in table 3 This indicates a relative deficiency in the teaching of pathology in most institutions The poor results noted in examinations on clinical dermatology were seen predominantly in candidates who received their clinical training largely by didactic methods There was also some indication that the teaching of syphilis and, to a lesser degree of physical therapy and mycology is deficient in some institutions

TABLE 2—*Comparison of Average Marks of A and B Candidates* at Various Age Levels*

Age	A	B
25 35		83 2
36-45	81 0	79 7
46 +	78 3	

* Data are based on study of a sample of 244 candidates

TABLE 3—*Relative Frequency of Failure, by Subjects, for 211 Candidates*

Subject	Number Failing	Percentage Failing
Pathology	134	63 0
Clinical cases	53	24 0
Syphilis	47	22 0
Physical therapy	43	20 0
Mycology	37	17 0
General dermatology	30	14 0
Allergy	14	6 5

TABLE 4—*Grades Made by Students with Varying Amounts of Training and Under Preceptors**

Under Preceptors	Total Amount of Training: Less than Two Years	Two to Three Years	Over Three Years
None	76 7	81 2	82 6
1 to 6 months	81 2	77 7	82 0
1 year +	80 4	79 8	82 1

* Data were gathered from a study of 178 candidates

The candidates who received part of their training under preceptors did as well in the examinations as those receiving hospital training only, when the total period of training was prolonged This observation would suggest that factual knowledge may be obtained equally well with part time preceptorship as with full time institutional work (table 4) as long as the candidate receives a total of at least three years of training

1 This group includes all candidates conditioned or failed and an additional sample of those who were given passing marks despite deficiencies in single subjects

A SURVEY OF TINEA CAPITIS, INCLUDING FAVUS

JACOB H SWARTZ, M D
Assistant Professor of Dermatology, Harvard Medical School

ETHEL M ROCKWOOD, M D
Assistant Dermatologist, Massachusetts General Hospital
AND
EARL A GLICKLICH, M D
Assistant in Dermatology, Massachusetts General Hospital
BOSTON

TWENTY-SIX years have elapsed since the publication of the last report from the Massachusetts General Hospital on the incidence of tinea capitis The only studies on this subject made at the hospital previous to the present report were presented by White,[1] in 1899, and by Greenwood,[2] in 1923

The purpose of this paper is to report a study of 288 cases of tinea capitis including favus The survey covered a period of six years beginning Jan 1, 1941 and ending Dec 31, 1946 During that period we observed no epidemic of tinea capitis

The species of fungi involved and their incidence in the series are presented in table 1 The findings compare with those of Greenwood,[2] who observed Microsporum lanosum in 67 5 per cent, Microsporum audouini in 25 per cent and Trichophyton schoenleini in 7 5 per cent of cases It may therefore be concluded that no change occurred in the relative incidence of M lanosum and M audouini in cases of tinea capitis recorded at the Massachusetts General Hospital in twenty-five years White,[1] however, in a series of 279 cases of ringworm, reported M audouini as the predominant organism, M lanosum was not mentioned Since White's report, which was published fifty years ago, a pronounced shift has taken place in the incidence of the different species causing tinea capitis in the same locality Of course it must be taken into account that the hospital draws its patients from a much larger area than formerly

Read before the Sixty-Seventh Annual Meeting of the American Dermatological Association, Inc, Murray Bay, Quebec, Canada, June 2, 1947

1 White, C J Ringworm as It Exists in Boston, J Cutan Dis **17** 1-17 1899

2 Greenwood A M Report on Cultures of Parasitic Fungi Arch Dermat & Syph **8** 81-82 (July) 1923

69 1 per cent of the total (852) now practicing in the United States Since the ratio of population of these thirty-one cities to the total population of the United States is 21 2 per cent, it will be seen that 69 1 per cent of the total number of certified dermatologists are serving only 21 2 per cent of the people in this country

The location of physicians who graduated from foreign medical schools and are now practicing dermatology in the United States is a matter of interest The total number in this group is 83 Of these, 53 or 64 per cent, are located in New York city Thus, more than 25 per cent of certified dermatosyphilologists in New York city graduated from foreign medical schools, and most of these persons are of foreign extraction as well Seven per cent of the group settled in Chicago, 3 of them are in San Francisco, 2 each are in Boston and Los Angeles, and the other 17 of this group are scattered throughout the country

There are 37 women who are certified specialists of the American Board of Dermatology and Syphilology Of these, 18, or nearly 50 per cent, are in New York city or its environs, 5 are in Chicago, 2 each are in Los Angeles and San Francisco, and the remaining 10 are scattered throughout the country

The number of dermatologists certified by the American Board of Dermatology and Syphilology, by state and geographic divisions, is given in table 6 The concentration of dermatologists in the Middle Atlantic States is seen to be twice that of the Pacific region and of the East North Central geographic regions which are second and third, respectively On the contrary the per capita distribution of dermatologists in the East South Central and in the Mountain regions of the United States is grossly inadequate The West North and South Central areas and the South Atlantic region are also in need of additional dermatologists

A further analysis of the data regarding the distribution of dermatologists in smaller cities in most parts of the country showed that the relative number of dermatologists was much smaller there than in larger centers It would be most desirable, therefore, for new certified specialists to consider seriously the advisability of settling in smaller communities In spite of the lamentable shortage of qualified dermatologists in the small and the medium-sized cities, particularly those serving predominantly rural areas, the majority of recent certified specialists start practice in already overcrowded metropolitan centers The explanation would appear to consist in a desire on their part to be affiliated with a university center, a wish for the availability of medical libraries and society meetings and, perhaps, in many instances, a response to the lure of a large city Inevitably, the law of supply and demand will force many of these younger men to move to the smaller communities It is an appealing fact that the need for adequate der-

Negroes In this series, culture in 96 2 per cent of cases yielded M audouini, 3 1 per cent M lanosum and 0 7 per cent M fulvum

Benedek and Felsher [6] reported a series of 140 cases of tinea capitis in Chicago, in which the causative organisms were as follows M audouini, 81 5 per cent, M lanosum, 12 2 per cent, not specified 1 4 per cent, T crateriforme, 1 4 per cent, Achorion schoenleini (T schoenleini), 1 4 per cent, and Achorion gypseum (M fulvum) 2 1 per cent The incidence in the report is at wide variance with our findings In our series the percentage of Negroes was negligible whereas in the series of Livingood and Pillsbury and in that of Benedek and Felsher it was high This may account for the difference

TABLE 2.—*Incidence of Tinea Capitis According to Sex*

Sex	Number of Cases	Percentage
Male	165	62
Female	101	38
Totals	266	100

TABLE 3.—*Incidence of Species of Fungi According to Sex in 256 Cases*

		Species			
		M Audouini		M Lanosum	
Sex	Total Number of Cases	Number of Cases	Percentage	Number of Cases	Percentage
Male	156	55	75	101	55
Female	100	18	25	82	45
Totals	256	73	100	183	100

Shaw [7] in a report on tinea capitis in southeastern Tennessee stated that from July 1942 to February 1946 22 patients were seen Three were Negroes and 19 white persons, 95 5 per cent of the patients were infected with M lanosum, 0 5 per cent with the genus Trichophyton and none with M audouini

Sixty-two per cent of the patients with tinea capitis exclusive of favus in our series were males (table 2)

The striking predominance of M audouini in the male sex—a ratio of 3 1 (table 3)—corresponded with the findings of other observers [8] The incidence of M lanosum was almost equal in both sexes

6 Benedek T, and Felsher, M Epidemiology of Tinea Capitis I Study of Tinea Capitis in Dispensary, Arch Dermat & Syph **49** 120-123 (Feb) 1944

7 Shaw, C Tinea Capitis in Southeastern Tennesse, Arch Dermat & Syph **55** 258-259 (Feb) 1947

8 Lewis and Hopper [3] Livingood and Pillsbury [4] Benedek and Felsher [6]

matologic care is nowhere more acute than in these smaller communities, where the young dermatologist has the best opportunity to render a superior service

STUDENTS IN TRAINING

There are at this time 488 dermatologic trainees in approved institutions in the United States Provided that the present rate of training continues, approximately 150 new dermatologists may be expected to start practice each year Even with the normal rate of attrition taken into consideration, the number of dermatologists in the United States in ten years will be more than doubled The greatest need at this time, then, is for dermatologists trained to be clinicians to serve in smaller communities, and, therefore, training in practical dermatology should receive the greatest emphasis in most instances It has been shown in the current study that formal lectures and demonstrations are insufficient for uniform attainment of proficiency The more individualized the training, the better the results, particularly in the clinical subjects The time has now arrived for dermatologists to be trained by means of the utilization of modern methods

WHAT OF THE FUTURE?

Since there is no unanimity of opinion with regard to the optimum number of physicians needed in the United States, it is difficult, if not impossible, to estimate the number of dermatologists needed to provide specialist care During and after the last war an emergency existed, and many veterans were trained in institutions with overexpanded facilities and in temporarily approved centers Payment of tuition and a sum for maintenance, by government subsidy, has made possible the training of many additional students Recently, two temporarily approved centers disbanded, and others may follow suit The aim of chiefs of service should be to stress quality of training rather than quantity of graduates If this precept is adhered to, the level of graduate teaching in some institutions will be elevated above the present standard It may be that the number of dermatologists who can be trained adequately each year may more nearly approach 100 than the present figure of 150

It is generally agreed that interest in and approval of teaching centers by the specialty boards have contributed singularly to the elevation of standards of practice There would seem to be little justification for any relaxation of interest by the boards if present standards of opportunities for students are to be maintained However, there is some basis for argument regarding the present stipulation of the American Board of Dermatology and Syphilology that all students must spend three full years of training in approved institutions before they may

required this treatment All patients with tinea capitis were treated with local therapy and manual epilation before being referred for epilation by roentgen radiation It is therefore unwise to assume,



Fig 2—Favus of the scalp and glabrous skin with typical scutula in the patient in case 1



Fig 3—Favus of the scalp in the mother of the patient in case 1

once M lanosum is cultured, that the disease will be nonresistant and will yield to local therapy alone

The cases of favus presented were in patients whose family histories included other cases with involvement of the scalp, glabrous skin and finger nails

My question then is, would it be possible for a thesis in some such selected scientific field of endeavor to be made additional material which could be presented to the Board and would then receive due consideration as a part of the candidate's qualification for a certificate? Not that one wants to make two classes of dermatologists—those who are scientists and those who are not—but some of the most valuable and promising students really would prefer to be freer from the cramming and rote learning in order to engage in investigative work and more fundamental studies Having to prepare for the Board examination takes so much of the student's time and energy in the graduate schools that it really requires a most unusual amount of strength and drive and love for science to enable a student both to prepare for the examinations and to do the collateral reading and study and actual research necessary for those who are to become leaders and teachers

Dr George M Lewis, New York The importance of certification by the Board has probably been overemphasized, although there is little doubt that there has been a progressive betterment of standards It is indisputable that dermatologists beginning their practices are better equipped now than formerly Perhaps the present emphasis should be mainly on selection of candidates for training who are found to have superior preliminary qualifications It would appear that the chiefs of service of approved institutions should realize the seriousness of providing the initial facilities for training, since most students complete their training once they have started

This paper is not an official document of the Board It represents the views only of ourselves It is also a pleasure to acknowledge the considerable help of Dr C Guy Lane, who, as former secretary of the Board, kept meticulous records which provided a source for a great deal of the data used in this paper

The Board is rightly placed in the position of being independent and yet is extremely sensitive to the wishes of everyone connected with the specialty On reflection, I am sure that those present here would wish it to continue to be independent In matters of policy the Board acts as a unit, and decisions are not made by one member of the Board The secretary would appreciate hearing from anyone regarding the Board activities and welcomes constructive criticism. It is requested that communications in regard to matters concerning the Board be addressed to the secretary and not to the individual members of the Board

There are many schemes for training the candidates, and the Board is sympathetic to most of these Some institutions stress training by means of didactic instruction, while others favor a more informal approach It would seem at this time that residency training is in the ascendency The Board does encourage training in which the student has the opportunity to carry on research during the period of his training At the same time, there is a considerable amount of basic knowledge that must be acquired It has been found that three years of conscientious training are required in order for the average student to become well grounded in the fundamentals of modern dermatology and syphilology

as deformed finger nails, and that his maternal great-grandfather, who had been born in Canada, had had crusting and scarring of the scalp

Physical examination of the patient's scalp disclosed yellow-brown crusts (some pierced by hairs), scarring and loss of hair The odor emanating from the scalp was offensive The clinical picture was characteristic of favus The face and the upper part of the trunk showed typical scutula (fig 2)

Examination of the mother's scalp revealed extensive scarring, with areas showing loss of hair intermingled with yellowish crusting (fig 3) The grandmother had burned-out favus of the scalp, the finger nails showed discoloration and deformity (fig 4) The toe nails were uninvolved

Results of microscopic examination and positive cultures of material taken from the affected hairs, nails and skin were characteristic of T schoenleini (figs 5, 6 and 7)

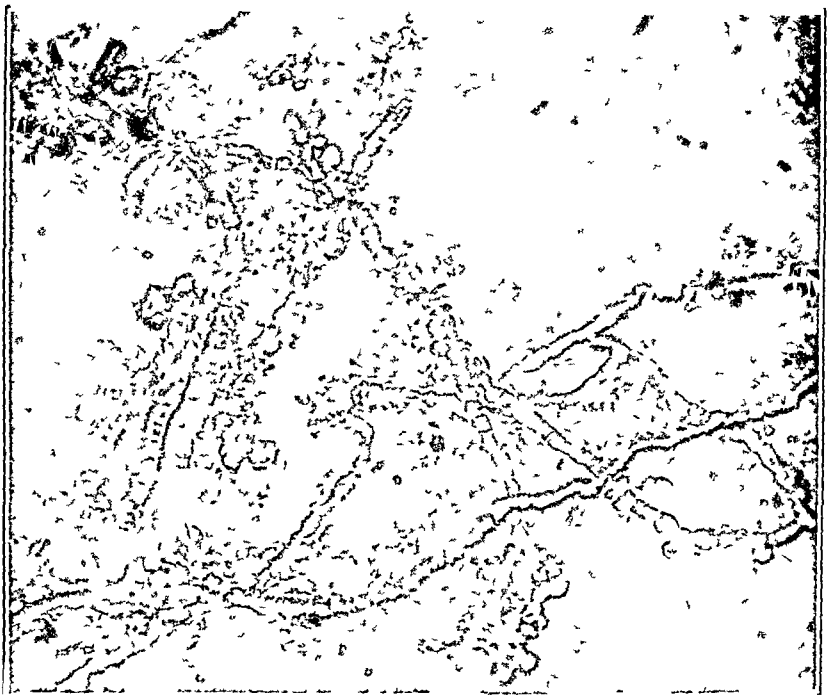


Fig 6—Direct photomicrograph of material from finger nails, indistinguishable from that in tinea unguium caused by organisms other than T schoenleini

Case 2—F V,[9] a boy of 14 born in Massachusetts, reported to the clinic on May 4, 1944 because of a scalp condition of ten years' duration The patient's mother, who had been born in Massachusetts, as well as the maternal grandparents and great-grandparents, who had been born in Canada, had had a similar condition

Physical examination disclosed scattered yellow-brown crusts on the scalp but little scarring or loss of hair A brother and a sister showed a similar picture A 17 month old brother had a crusting and scaling patch on the vertex of the scalp

Direct microscopic examination and cultures confirmed the clinical diagnosis of favus

9 This patient was referred by Dr L A Anderson of Springfield, Mass

Lewis and Hopper [3] reported the causes of tinea capitis as observed in the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, in a series of 292 cases covering a period from 1935 through the first six months of 1938 The data were M lanosum, 39 6 per cent, M audouini, 39 3 per cent, Trichophyton violaceum, 7 5 per cent, T schoenleini, 5 8 per cent, Trichophyton crateriforme, 1 7 per cent Microsporum fulvum, 1 0 per cent, Trichophyton gypseum, 0 3 per cent, and undetermined species, 4 7 per cent The series included an epidemic of 15 cases, all due to M audouini If these are omitted, the incidences of M lanosum and M audouini become 42 2 and 34 1 per cent, respectively These findings indicate that except in an epidemic M lanosum is responsible for the greater number of cases of tinea capitis in New York as well as Boston An increase of cases due to M audouini, however, has been observed in the last three years In the series of Lewis and Hopper the genus Trichophyton, exclusive

TABLE 1—*Incidence of Species of Fungi in 288 Cases of Tinea Capitis*

Species	Number of Cases	Percentage
M lanosum (M canis)	188	65 3
M audouini	73	25 4
M fulvum (M gypseum)	2	0 7
T schoenleini	22	7 6
T gypseum (T mentagrophytes)	2	0 7
T sulfureum	1	0 3
Totals	288	100 0

of T schoenleini, was present in 9 8 per cent of cases, as compared with 1 per cent in the present series T schoenleini was found in 7 6 per cent of the cases in the present series, as compared with 5 8 per cent in that of Lewis and Hopper The higher incidence of the species in this survey is probably due to the inclusion of the two families with cases of favus in four generations of each

In Weidman's [4] report of 36 cases in Philadelphia, it was noted that cultures from 50 per cent of patients yielded M lanosum, 41 7 per cent M audouini and 8 3 per cent other species

Livingood and Pillsbury [5] reported 130 cases of ringworm of the scalp in persons from families in the lower economic stratum of central and south Philadelphia Ninety-six per cent of the patients were

3 Lewis, G M, and Hopper, M E Introduction to Medical Mycology, Chicago The Year Book Publishers, Inc, 1943

4 Weidman, cited by Livingood and Pillsbury [5]

5 Livingood, C S, and Pillsbury, D M Ringworm of Scalp Prolonged Observation, Family Investigation, Cultural and Immunological Studies in One Hundred and Thirty Cases, J Invest Dermat **4** 43-57, 1941

M lanosum, but it should be noted that in a fairly high percentage of the cases caused by M lanosum the condition did not respond to the routine local treatment and manual epilation used in the clinic before roentgen epilation was employed

Cases of favus in two families of four generations each are reported In one case there was involvement of the finger nails, and in another involvement of the glabrous skin All the patients had involvement of the scalp In one family three generations and in the other two generations had been born in the United States

ABSTRACT OF DISCUSSION

DR ANDREW M DAVIDSON, Winnipeg, Manitoba, Canada In the series of cases of tinea capitis including favus in the city of Winnipeg, the frequency of M audouini was three times as great as that of M lanosum, but the series covered the period of an epidemic due to M audouini

This epidemic was cleared up eleven years ago, another case due to M audouini was not reported until last year, when 3 children, one of school age, in a family which had moved from Calgary, Alberta, were all found to be infected with M audouini

The incidence of cases of tinea capitis caused by M lanosum has remained at about the same level, but this type has come mostly from the country areas Those cases due to T gypseum, T violaceum or Trichophyton album (T schoenleini) are much less frequent, this type also comes from the surrounding farming country, usually in the form of kerion

I have been especially interested in tinea capitis of the human type in the city schools and orphanages During the epidemic from 1932 to 1936, the problem was successfully tackled with the support of the city medical officer of health

Ringworm of the scalp was made a notifiable disease, and infected children were excluded from school All patients were treated in the department of dermatology of the Children's Hospital in Winnipeg The school nurses were supplied with inexpensive, homemade portable lamps with filters of Wood's glass In every school where disease of the scalp was discovered, all children filed through an emergency darkroom, where they were examined with Wood's lamp

Those infected with ringworm were isolated, the diagnosis was later verified in the Children's Hospital, where a water-cooled quartz lamp was installed for this purpose Children in the orphanages were similarly examined

A competent mycologist from England made a study of the cultures on French proof agar The first cultures were verified by Dr Howard Fox and Dr Muskatblit of New York Samples were then sent to the Central Bureau, in Holland, and the Manitoba type cultures were registered Later in the investigation, all cultures were verified by the hyphal fusion method described by Professor Buller This method was applicable to the dermatophytes, as to other fungi Myceliums from similar species show hyphal fusions, those from different species do not

The children infected with M audouini were treated by roentgen epilation

Dr Swartz stated that in 37 3 per cent of the cases in his series due to M lanosum the condition did not respond to local treatment

There were no resistant cases in the series in Winnipeg after adoption of the plan of hospitalizing all patients with ringworm of the scalp, this was probably due to more thorough treatment than had been carried out in the patients' homes

As indicated in the accompanying chart the age was recorded in 257 cases The youngest patient in the series was 6 months old and the oldest 20 years Three were between the ages of 14 and 20 The greatest incidence of the disease was at the ages of 6 and 7 The average age was 6 years 2 months

It is interesting to note that some of the patients with tinea capitis who were at the age of puberty showed lack of physical signs of maturity This was exemplified in one family in which 2 brothers were affected in the following manner tinea of the glabrous skin only was observed in the case of a boy of 11½ who showed physical signs of maturity, whereas his brother, who was 13½ but did not show signs of maturity, had tinea capitis It may be of value to study adults with tinea capitis from the point of view of production of androgens

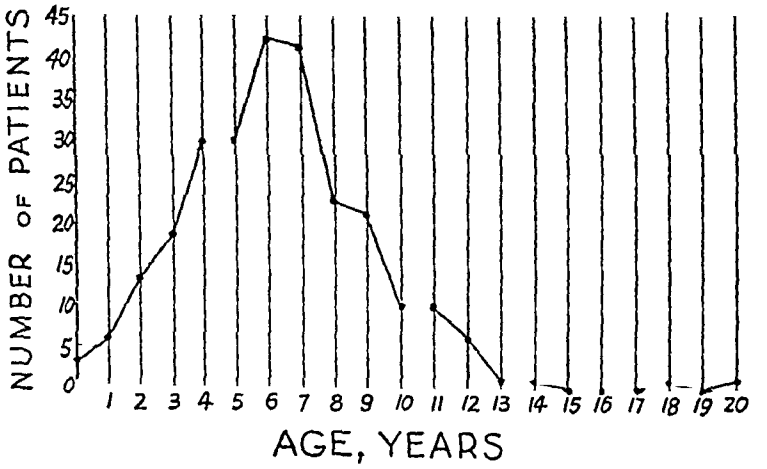


Fig 1—Incidence of tinea capitis according to age in 257 cases

Of the patients in 266 cases of tinea capitis not including favus, 59 (22 2 per cent) required treatment with epilation by roentgen radiation (table 4)

TABLE 4—*Cases in Which Roentgen Epilation Was Required*

Organism	Number of Cases	Percentage
M lanosum	22	37 3
M audouini	32	54 2
Trichophyton (various species)	1	1 7
Unidentified	4	6 8
Totals	59	100 0

Although the highest percentage of cases in which patients required epilation by roentgen radiation were due to M audouini (54 2 per cent), 37 3 per cent of patients with tinea capitis caused by M lanosum also

Dr Oliver told me that he was getting good results with local treatment and was abandoning the use of roentgen epilation Improved results with local treatment may be due in part to better care of children since the war and to the fact that the epidemic is undoubtedly dying out My experience indicates that the infection was not spread at barber shops but was carried on seats in public conveyances and motion picture theaters Most of the children infected were small, and their heads would have rested against the backs of the seats

Infection was seven times more common in boys than in girls Some of the girls I saw with the infection parted their hair in the middle and had pigtails, offering ideal surfaces for contact

I have not had much success with local treatments I have tried them all from time to time and have finally resorted to epilation, which in my experience has been the most satisfactory method of treatment I have not tried treatment with androgens, but I believe Dr Rattner has had considerable experience with such methods

I should like to show slides of a series of cultures, illustrating a crude method of evaluation of various fungicides [Slide] The first view illustrates the control All the cultures were made with hairs from the same lesion of the scalp The second culture was made with a soap, supposed to be effective The next was made with a mixture of equal parts of phenol and camphor, an inert preparation except when water comes in contact with it and thereby liberates the phenol The fourth was made with a similar mixture of phenol and camphor, to which water has been added, and the next with benzalkonium chloride U S P (zephiran chloride®) The next two cultures were made with sopronol ointment® (a water-soluble ointment containing sodium propionate 12 3 per cent, propionic acid 2 7 per cent, sodium caprylate 10 per cent, zinc caprylate 5 per cent and dioctyl sodium sulfosuccinate 0 1 per cent) The last was made with phenyl mercuric salicylate, a preparation which kills everything within reach but is extremely irritating I have used it with a 1 per cent solution of acetone in infected scalps with some benefit

[Slide] Here is the much advertised zincundecate (desenex®) The hairs were embedded in the ointment No attempt was made to clean the ointment off the hairs, they were merely planted on a surface of French proof agar M audouini seemed to grow a little better with desenex® than without

[Slide] The next views are of cultures made from scales after treating a patient's foot, which I shall show you next The foot was treated for two weeks with desenex® without clinical improvement, and positive cultures could still be obtained from the tops of the vesicles I have failed in years gone by to get positive cultures after treatment with ointment of benzoic and salicylic acid N F (Whitfield's ointment), and I have long since discontinued routine culture after this treatment

[Slide] One serious complication occurred in the roentgen epilation The development of alopecia areata This was not due to errors in technic or use of the x-ray apparatus With the five point method the alopecia would have been at one of the five points, but in this case it was in the lower left part of the occipital area, which could not possibly have been overtreated with careful technic

Epilation in this case was done not in my office but at the Presbyterian Hospital, in January 1946 When I first saw the patient I was alarmed, but the family was cooperative I saw the patient a year later, after all the hair had grown in, and no further difficulty has developed at the time of this report

REPORT OF TWO CASES

CASE 1—P C, a boy of 6 who had been born in Massachusetts and whose parents and grandparents had been born in Massachusetts, reported to the clinic on Jan 6, 1944 because of loss of hair, crusting and scarring of the scalp and a

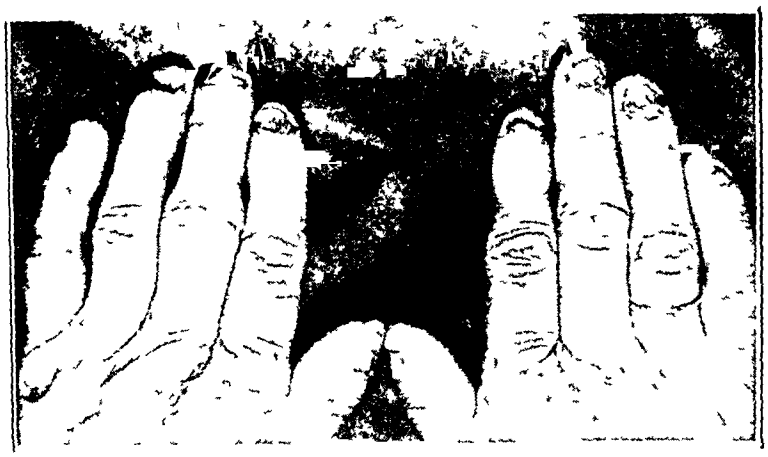


Fig 4—Favus of the finger nails in the grandmother of the patient in case 1

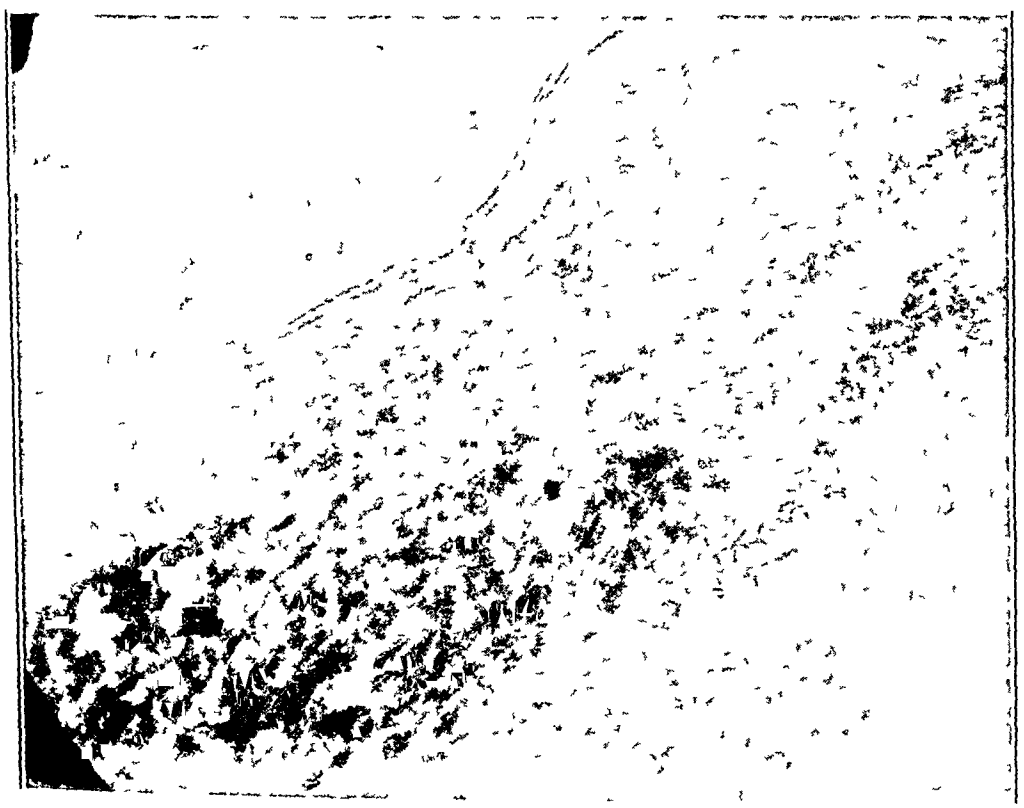


Fig 5—Direct photomicrograph of a hair, showing air spaces, myceliums and large spores in chains

rash on the face and the upper portion of the trunk The scalp condition had been present since the age of 1, and the glabrous skin had become involved within the past year

On further questioning, it was learned that the patient's mother had had trouble with the scalp, that his maternal grandmother had had scars on the scalp, as well

the regulations is supervised by a board of examiners, barbers themselves and elected by the barbers Therefore, the health department finds itself in the position of being assured by the barbers that regulations regarding sterilization are enforced Such assurances are inconsistent with the facts, a trip to any tonsorial establishment dispels the idea of sterilization in practice There is not the slightest attempt at sterilization Barbers would be anxious to sterilize their instruments if they thought it important, but they will not engage in methods of sterilization which are time consuming and which interfere with their livelihood Many barbers disapprove of the method recommended by the United States Public Health Service, as there are objections to immersing clippers in oil Sterilization by vaporization is impractical Therefore, when one approaches a group of barbers and asks, "What type of sterilization would you consent to adopt?" they reply that they would like a method which is brief and effective, by which sterilization could be accomplished within half a minute

With this request in mind, I consulted an inventor and an engineer and requested that they design an instrument which would blow a blast of hot air onto a pair of clippers and thoroughly clean the instrument (Preliminary tests in our tinea capitis clinic indicate that it is possible to sterilize instruments with brief blasts of dry heat at high temperatures) The first model was large and unwieldy A second, smaller model is now being made When it is completed, I hope to present to the barbers a small sterilizer, which requires only the insertion of a pair of clippers and the turning of a switch, a blast of hot air will then blow all the hairs from the clippers and suck them down into a collecting compartment

DR MAMNETT A DIXON, Toronto, Canada In Toronto, at the Hospital for Sick Children, cultures have been made with material from patients with ringworm of the scalp Fifty per cent of the cultures, from 36 patients to date, have shown M audouini and 50 per cent have shown M lanosum

DR JOHN G DOWNING, Boston I believe that if Dr Swartz were to compute yearly incidence he would find that in the past few years there has been a change in the fungus primarily responsible for this disease Mycologic studies, made in the laboratory of the Boston City Hospital during the eighteen month period from Nov 1, 1945 to May 1, 1947, indicate that the incidence of various fungi in 115 positive cultures was as follows M audouini, 68 (approximately 60 per cent), M lanosum, 44 (38 per cent), and T schoenleini, 3 (2 per cent) Of these 115 patients, only 6 were girls, 5 of the girls were Negroes The girls' lesions had first appeared in the bald areas left by tight braiding The average age of all patients at onset of the disease was 6½

Forty-six cases were followed for a sufficient length of time to evaluate treatment and prognosis Clinical cure was determined after negative results in 3 weekly fluorescence tests, plus negative cultures Tinea capitis due to M lanosum, regardless of the type of treatment, was pronounced cured on an average in less than three months Eighteen per cent of the infections due to M audouini were cured by local treatment alone, without roentgen radiation Thymol in chloroform was used in 3 cases due to M audouini, 2 patients were pronounced cured If these 2 cases had not been considered, the number would have been near 10 per cent, the figure for spontaneous cures reported by Dr Lewis Of the 3 patients with favus, 2 were mother and son in one of the families in Dr Swartz's report, these 2 had had the disease for years The third patient was a friend of the son, who had been afflicted for one year and showed a single patch In 1944, Morris reported a cure in 2 cases of infection due to T schoenleini in which a 10 per cent solution of thymol in chloroform was used (*New England J Med* **230** 667-669 [June 1] 1944) The patients are well at the time of this report

These cases are presented because of the presence of favus in the two families for four successive generations, the presence of favus in members of one family for three successive generations born in the United States and the presence of favus involving the glabrous skin and the finger nails

SUMMARY

A study of the incidence of species of fungi in cases of tinea capitis recorded in the dermatologic clinic of the Massachusetts General Hospital reveals that M lanosum is responsible for the majority of cases (65 3 per cent)

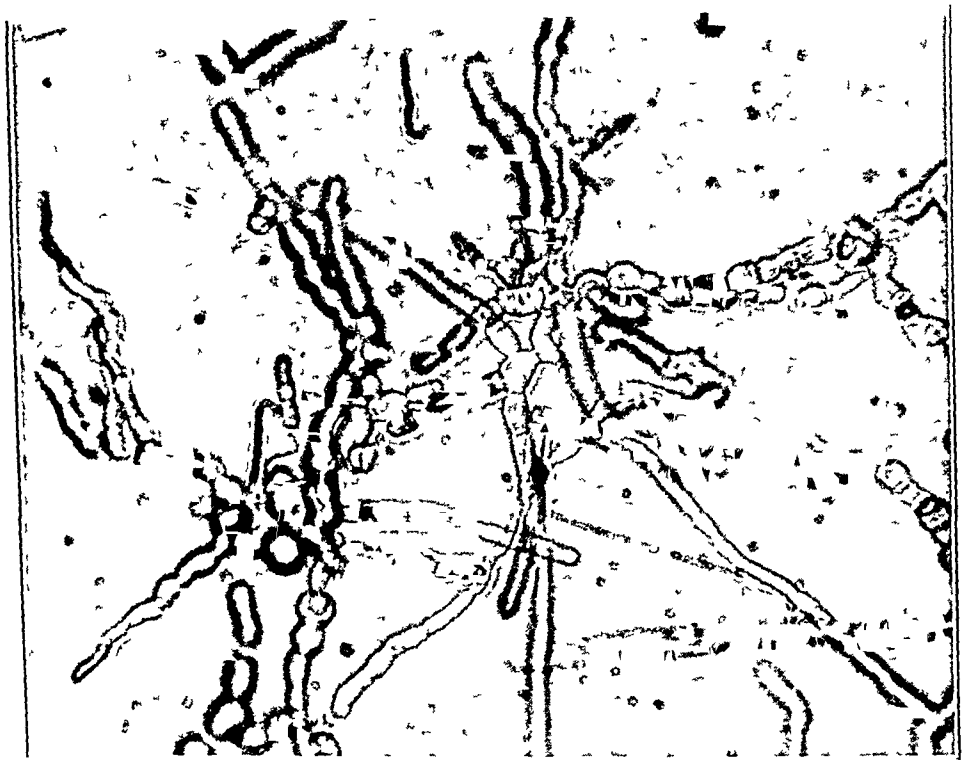


Fig 7—Culture mount, showing "favic chandeliers" and chlamydospores

One and a half times as many males as females were seen with tinea capitis M audouini was observed three times as often in the male patients, whereas M lanosum was observed almost equally in both sexes

In this series, the youngest patient was 6 months and the oldest 20 years The average age was 6 years 2 months

It is believed that a study of production of androgens in adults with tinea capitis would offer the opportunity of valuable findings

Treatment by roentgen epilation was resorted to in 22 2 per cent of cases, of which 54 2 per cent were caused by M audouini and 37 3 per cent by M lanosum (cases of favus were not included in this group) The figures confirm that tinea capitis caused by M audouini is more resistant to treatment than the form caused by

HYPERTROPHIC DARIER'S DISEASE AND NEVUS SYRINGOCYSTADENOMATOSUS PAPILLIFERUS

Histopathologic Study

HERMAN BEERMAN, M D
PHILADELPHIA

TWO RECENT events emphasize the desirability of resurveying certain of the histologic appearances of Darier's disease (keratosis follicularis) The first is the recognition of familial benign chronic pemphigus and its separation from the concept of Darier's disease (by Hailey and Hailey, and others) The other is the following experience involving a number of competent pathologists, both dermatologic and general In the course in pathology given by Weidman at the American Academy of Dermatology and Syphilology in Chicago in 1940, an "unknown" slide (3675) was included among those of the tumors as an example of Darier's disease, with pseudoepitheliomatous hyperplasia When this slide was presented to the round table on pathology at the same meeting, those present stated the belief that the specimen represented nevus syringocystadenomatosus papilliferus Since then, the specimen has gone the rounds, and considered diagnoses have varied from atypical squamous cell epithelioma, to a combination diagnosis, such as, "At one edge of the section there were changes suggestive of Darier's disease, in the middle, there were changes that looked very much like adenoma hidradenoides (Perthes) as depicted in Gans's Histology of Diseases of the Skin,' volume 2, page 279, in places, this type of change went over to frank basal-squamous cell epithelioma" It is my purpose, therefore, to review briefly the basic histologic features of Darier's disease, to demonstrate that pseudoepitheliomatous hyperplasia of basal cells is an essential feature of this disease, especially in the papillomatous form, and to establish criteria for the histologic differentiation of this unusual variety of Darier's disease from a nevus of the sweat apparatus

VEGETATING DARIER'S DISEASE REPORT OF CASES

In addition to the specimen from the case (slide 3675) presented by Weidman, as noted previously, my associates and I have studied for the past seven years another extreme example of the vegetating

Read at the Sixty-Seventh Annual Meeting of the American Dermatological Association, Inc, Murray Bay, Quebec, Canada, June 2, 1947

From the Department of Dermatology and Syphilology, University of Pennsylvania School of Medicine, Donald M Pillsbury, M D, professor

The most important part of the treatment was the continued use of Wood's lamp for the detection and removal of all infected hairs Because of this, no child returned to school until the cure was complete

Physicians in Winnipeg have been fearful of another epidemic of M audouini, and my colleagues have been on the watch for any immigrants with ringworm There have been epidemics in Vancouver, British Columbia, Calgary, Alberta; Ottawa, Ontario, and Minneapolis

Our experience may be summarized as follows Ringworm and favus should be notifiable diseases under the control of a public health authority, careful studies of cultures of the fungi are essential for correct diagnosis, infected persons should be isolated until cure is proved with Wood's lamp, epilation should be the responsibility of a dermatologist experienced in this work, the establishment of a department to eradicate ringworm in school children, which includes persuasion of the powers that be, is a task of the first magnitude

DR JAMES HERBERT MITCHELL, Chicago .For the December 1946 meeting of the American Academy of Dermatology and Syphilology I attempted to make a survey of tinea capitis on the entire North American continent With a few exceptions my sources of information were private

The declining epidemic of ringworm originated in New York city I was unable to get any cooperation from health departments, but individual physicians later sent me various figures, which show that the epidemic traveled straight across the country

Dr Swartz has stated that there were no signs of the epidemic in Boston Drs Pillsbury and Livingood said the same as regards Philadelphia However, in crossing the country, the epidemic hit Syracuse, Rochester and Buffalo in New York state and Ann Arbor and Flint in Michigan, and in Chicago it became a real menace Probably 6,000 or 7,000 cases have been recorded in Chicago

The original survey of the schools in Chicago indicated that 2 6 per cent of all public school children examined were infected The survey for the first five months of 1947 indicated that infection was present in only 0 6 per cent of more than 200,000 children who were examined by the health department I was unable to get any figures on the cases reported by Chicago physicians to the health department, which does not seem to be able to cope with the situation

The epidemic was mild in Eastern Canada and did not extend to Western Canada It went south more or less directly

In my experience, the causative agent in this epidemic has almost invariably been M audouini I have found only 1 instance of T violaceum and 1 of M lanosum, material from the latter was sent to me from Springfield, Ill, for culture

It is interesting to note that the Southeastern states were more or less spared except for the northern part of Virginia and in Richmond I do not know why The epidemic was severe in the Twin Cities, but it was not much of a problem in Kansas City, Mo It gradually died out while going westward and ceased to be a problem on the West Coast

Dr Davidson has stressed the importance of making ringworm of the scalp a reportable disease In Anderson, Ind, a town of 42,000, there were 432 cases at the peak The commissioner of health, Dr E M Conrad, has carried on a most energetic campaign to stamp out the disease He has just reported to me that in the first five months of this year there have been no new cases

Dr Moore made the statement in 1941 that he knew of only 4 cases of infection with M audouini in St Louis He estimates, at the time of this report, that there are at least 4,000 cases due to M audouini in St Louis

center of the section, the general principles in the construction of a lesion of Darier's disease could be identified, but they had developed on a gigantic scale For example, hyperkeratotic villosities projected on the surface, and between them, at their bases, the lacunas could be identified It was at this point that a puzzling picture obtruded in the form of a pseudoepitheliomatous hyperplasia proceeding from the floor of the lacunas

"The pseudoepitheliomatous hyperplasia ranged from small to huge infiltrations Mitotic figures were abundant At times small pearly bodies appeared. Occasionally a psorosperm could be identified, and at one place foreign body giant cells were disposed around scraps of keratinous material Most interestingly, empty clefts appeared rather consistently within this pseudoepitheliomatous material, thus indicating the preservation of the tendency to repeat the architecture (papillary) which so commonly appeared at the base of the lacunas at the surface.



Fig 2 (case 1) —A close-up view of vegetating lesions in the anal cleft and perineum

Indeed, it was this feature, rather than the more usually emphasized psorosperms, which identified the changes here as those of Darier's disease Much of the pseudoepitheliomatous tissue lay below the level of the sweat glands and even attained the deep arterial plexus

"This was a most unusual expression of Darier's disease because the psorosperms were so inconspicuous, in spite of the highly developed stage of the lesion Indeed, the diagnosis was prompted more by the formation of lacunas, albeit atypical There was a tremendously exaggerated hyperplasia of the tissue which ordinarily comprises the floor of the lacunas, resulting in its extension of the tissue to the deepest parts of the corium Thereupon the question of whether or not a true cancerous change had taken place had to be met

"I was extremely loath to make a diagnosis of cancer in any case of Darier's disease, in view of clinical knowledge I felt thus especially when I considered what was known of the range of the possibilities of pseudoepitheliomatous hyper-

DR EDWARD A OLIVER, Chicago As Dr Mitchell has said, the prevailing organism in Chicago has been M audouini

Roentgen epilation is not always wanted by the parents of patients and is difficult to use in the smaller communities when expert technicians are not at hand Dr Felsher, of Northwestern University, has just completed a study of 150 cases caused by M audouini in white children He used the ointment originally suggested by Dr Schwartz

Dr Felsher effected a cure in 105 cases in the group The shortest period required for cure was three months and the longest fourteen months, the average was six and a half months Eight patients, whose infection was limited to one fourth of the scalp, were cured in an average of five and a half months Of the patients with severe cases only 25 per cent recovered fully, in an average period of eight and a half months

Of the 45 patients not cured, the infections in 7 showed an improvement of less than 50 per cent Of the 38 patients whose infections improved over 50 per cent, improvement of 75 per cent was noted in 14 The severity of the disease, as manifested by the size and number of the lesions, was an important factor in determining the rate of recovery The duration of the disease before treatment was begun and the age of the patients had but little bearing on the time required for the cure

Unfavorable reactions to the ointment were not observed, it has proved superior to other topical applications They were all tried, including the use of androgens In the mild and moderately severe cases, this ointment gave results that compared well with those obtained by roentgen epilation However, roentgen epilation was superior in the very severe cases

DR C GUY LANE, Boston Some years ago I reviewed, with regard to the time of the children's return to school, a series of cases of tinea in which the patients were treated with roentgen radiation (The study was never published) During a period of four years, some 112 patients were treated with roentgen radiation Forty of these children were able to return to school in the fourth week, 37 in the fifth week and 35 in the sixth week

At the time when these children returned to school, they were not all checked with Wood's lamp and with cultures, but results of microscopic examinations were negative and the children apparently were clinically free of the disease

Around Boston there is considerable difference in the various communities with regard to permission for children to return to school Sometimes the matter is in the hands of the school physician and sometimes in those of the school nurses, and the decision depends on their interpretation of the rules of the board of health in the particular community

There ought to be a wider publication of reliable information with regard to the infectivity of ringworm and the conditions under which children may return to school I hope there will be wider publication of the report of the committee which studied the matter in New York under the chairmanship of Dr Lewis

With regard to the photograph which Dr Mitchell showed, since 1939 there have not, as far as I know, been any cases of permanent alopecia caused by roentgen radiation in Boston I have seen 4 patients with permanent alopecia, in 2 of these cases, as I recall, epilation was performed in Europe before the patient came to this country

DR MAURICE SULLIVAN, Baltimore I shall confine my comment to sterilization of instruments used in barber shops In Baltimore, conformance with

disease with possible nevoid changes on the forehead At the time of the patient's admission to the Hospital of the University of Pennsylvania, in 1939, the process had been present for seventeen years, having begun in 1922 as a "boil" on the perineum This had ulcerated and drained for several years In 1932 lesions had begun to appear on the sacral region These gradually had increased in size, and new lesions had appeared higher on the back Several years later the thorax had become affected, and in 1934 pustules had appeared on the sides of the nose The forehead had become involved in 1937, the retroauricular region in 1938 and the scalp, pubic region and axillas in about 1940 Previous treatments of various types had had no restraining effect on the lesions Proliferative lesions, previously removed, had recurred within several years The status of the patient's parents is unknown, but a brother is similarly affected A sister and 3 children are normal



Fig 4 (case 2) —A view showing lesions of the vegetative type on the face and scalp

The patient was admitted to the hospital on three occasions, in 1939, 1942 and 1946 During these admissions numerous studies were made There was no evidence of vitamin A deficiency, according to clinical examination and blood levels, nor was there any response to the oral administration of vitamin A, in a dosage of 250,000 units daily for a month Visceral examination revealed possible hypertrophic gastritis There was no response to roentgen therapy given to the pubic region in 1946, and surgical excision of some of the lesions of the ear and nose was done

The lesions occurred in a somewhat seborrheic distribution (figs 4 and 5), that is, on the scalp, the frontal, temporal and malar regions, the nose, ears and adjacent areas and the neck, in two deep V's extending over the sternum and on the abdomen anteriorly, between the scapulas and onto the lumbar region posteriorly

DR GEORGE M LEWIS, New York The present epidemic of tinea capitis presents to public health authorities a challenge which many have not seen fit to accept seriously Compared with other infectious diseases ringworm of the scalp, while not a menace to life, still commands respect because of its contribution to misery and because of the coincident economic loss There are many divergent views on different phases of its control, its insidious spread over the country being sufficient testimony to the ineptness, the lack of knowledge and, often, the lack of interest of many of our public health officials The hope that dermatologists will improve the therapy and that natural forces will operate sufficiently well for the disease to become less prominent would appear to be that of many city, state and federal public health workers who would hardly dare to be so casual about any other infectious disease

It would now seem that the local therapy advocated by Swartz and his co-workers may be slightly more effective than remedies which have been used previously and that, if persisted in for four months or more, it will effect a cure in a considerable proportion of cases While it is not to be considered as a specific, it does indicate that a chemotherapeutic remedy may eventually be found to control this infection satisfactorily

DR SAMUEL AYRES JR, Los Angeles The question of alopecia has been mentioned I have under my care a patient who was treated not for ringworm but for an epithelioma of the forehead, with 1800 r There was complete protection of all surrounding tissues

Within approximately two weeks, a typical patch of alopecia, with exclamation point hairs, developed behind the treated area

DR JACOB H SWARTZ I want to mention that I am not the Dr Schwartz whom Dr Oliver mentioned in connection with the course of treatment

I, too, want to stress the differences noticed lately in the cultures of M lanosum They are more difficult to identify on gross examination On culture mounts, the typical spindle-shaped fuseaux may be seen only in the old cultures

Our experience, unlike that of Dr Lewis, has been that the response to treatment has been poorer

We have completely stopped using thallium acetate because of the ill effects

To answer Dr Downing's report and suggestion, I have broken down my figures for the last three years and I have them here In spite of the fact that the percentage of cases due to M audouini has increased in the past three years, in 1944 there was still a predominance of M lanosum (44 2 per cent) over M audouini (36 2 per cent) In 1945 the percentages were M lanosum, 46 9, and M audouini, 41 1 In 1946 the trend had changed, and the percentages were M lanosum, 53, and M audouini, 34 Therefore, even though the relative incidence of M audouini has increased, there is still a predominance of M lanosum in our series

Specimens for biopsy were removed from the supraorbital region, right cheek, right bregma, ear and postauricular region, nose, hands, anal region and groin of this patient The pathologic changes varied from a very simple picture of Darier's disease, as exemplified by the lesion removed from the hand, to extremely complicated structures, as exemplified by the lesion removed from the supraorbital region



Fig 6 (case 2) —Section of a lesion from the hands, showing the usual features of a papular lesion "follicular" location, hyperkeratosis, corps ronds, acanthosis, lacunas and a slight tendency to basal cell proliferation (slide 952)

Section 952, removed from the hand, showed a verrucous surface with extensive hyperkeratosis, especially in epithelial invagination The granular layer was normal There were epidermal edema and moderate acanthosis The pigment in the basal layer was preserved, especially in the less acanthotic portions of the

type of Darier's disease Observations of these cases and material from a case of nevus syringocystadenomatosus papilliferus form the basis for this report

CASE 1.—The patient was a 40 year old nonleprous Negro at the United States Marine Hospital, Carville, La The late Dr Ralph Hopkins made the diagnosis of Darier's disease Through the courtesy of Dr Sam Black and Dr H E Hasseltine, Dr Weidman received a specimen from the perianal region,



Fig 1 (case 1).—A front view, showing the more or less usual papular form of Darier's disease in seborrheic distribution

as well as clinical photographs (figs 1 and 2) The process, nonpruritic, had been present for twenty years The essentials of Dr Weidman's microscopic description of the specimen are submitted as follows (fig 3) "The diagnosis of Darier's disease could have been made only with qualifications were it not for the presence of one or two very small lesions of Darier's disease at the extreme end of the section and on the surface In this location the typical lacunas and fairly good examples of psorosperms were observed Toward the

entire section There were a number of cornified cysts in the corium (Kreibich [2]) There was marked basal cell proliferation, showing mitotic figures, with lacunas above them In some sites this proliferation was extreme, as shown in figure 7 There were some chromatophores, a dense infiltration containing plasma cells and a number of dilated blood vessels in the corium There were abundant hairs in the specimen



Fig 8 (case 2) —A section from the perianal region Note the general structure, which resembles the histologic features of nevus syringocystadenomatosus papilliferus (slide 943, × 16)

Section 943, removed from the perianal region, showed a verrucous surface, extensive acanthosis and epidermal edema At one end of the section were

2 Kreibich Hyperkeratose (Kyrle) und Dyskeratose (Darier), Arch f Dermat u Syph **163** 215, 1931

plasia In this dilemma I had to concede that I had never seen the latter extend to such a deep position in the skin I could understand the presence of the pearly bodies and the mitotic figures

"All things considered, I decided against the diagnosis of cancer and should explain the deep position of the infiltration on the basis of the great mass of epithelial material which comprised the bulk of the lesion. The final answer must rest in the clinical course, pending which I should prefer to regard the changes

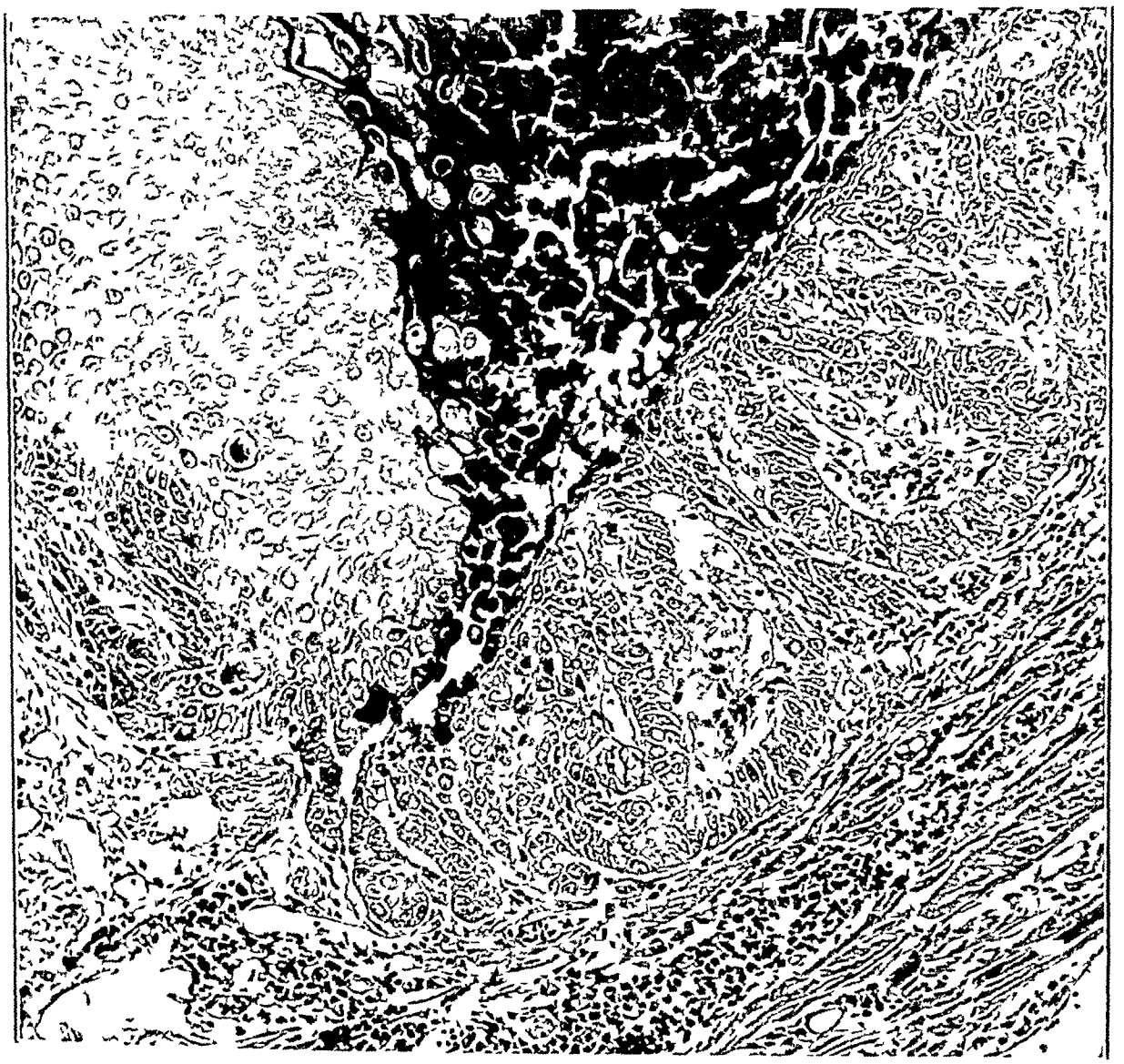


Fig 3 (case 1) —The histologic features of hypertrophic Darier's disease hyperkeratosis, corps ronds, grains, lacuna, acanthosis and, especially, basal cell proliferation Mitotic figures and a scanty inflammatory reaction in the corium may be noted (slide 3675)

as those of pseudoepitheliomatous hyperplasia rather than of the cancer which the condition appears to be"

Case 2—The case of M G, a white coal miner aged 43, was presented to the Philadelphia Dermatological Society in 1939 by Johnson [1] as an example of Darier's

1 Johnson, H M Darier's Disease, with Possible Nevoid Changes on the Forehead, Arch Dermat & Syph **41**.448 (Feb) 1940

Section 1988, removed from the groin, also had features similar to those of section 946 Metaplasia of the prickle cells (fig 10) lay side by side with proliferation of basal cells

Section 2689, removed from the right postauricular region, presented a picture similar to that of section 946, but there were lobules suggestive of glandular



Fig 10 (case 2) —Specimen from the groin, showing considerable hyperplasia (metaplasia) of prickle cells and basal cells (slide 1988)

carcinoma At high levels all the basal cell "acini" had surrounding lacunas These were really representative of cross sections of villous projections

Section 54631 showed histologic features similar to those of section 946 Exquisite corps ronds were to be noted

Sections 1559 and 2716 also showed changes essentially like those of section 946

in the axillas and the groins, over the pubis and in the gluteal cleft, and on the extensor, hairy surfaces of the forearms and the dorsa of the hands The palms had a diffuse, yellowish thickening, and the finger nails were spoon shaped Uninvolved portions of the skin were the bearded part of the face; the arms, thighs, legs and feet, the flanks and buttocks, and the external genitalia In 1941 the oral and rectal mucosae were normal, but in 1946 there were whitish plaques on the anterior pillars and tonsillar areas The rest of the oral mucosa was pale



Fig 5 (case 2) —Extreme hypertrophic lesions on the suprapubic region

An individual early lesion was a small, firm, discrete, rose or violaceous process at or near a pilosebaceous orifice Older lesions were larger, more elevated and purple, bronze or brown, and groups of them coalesced The surfaces looked waxy and displayed widened orifices, from many of which a long "worm" of thickened sebum might be expressed On the scalp, in the gluteal cleft and the groins and over the pubis, this piling up of tissue had caused the formation of tumor-like masses, punctuated with numerous gaping, glandlike orifices and deep clefts, from which the decomposed sebum and sweat gave forth a pungent odor The masses were so situated on the face that the patient had a leonine appearance, and their deep color caused a dusky hue

Histopathologic Characteristics Histologically, Darier's disease is essentially an epithelial process Outstanding features are peculiar cell degenerations (dyskeratosis, the so-called corps ronds and grains), hyperkeratosis and parakeratosis, acanthosis, lacunas and spaces in the epidermis and a pronounced basal cell hyperplasia The surface of the lesion is uneven and contains invaginations, which are filled with horny plugs The epithelium surrounding these horny plug–filled invaginations shows the aforementioned atypical proliferation of the basal cell layer In addition, there are pigmentary changes and minor alterations in the corium

Most dermatologists are familiar with the hyperkeratosis and parakeratosis found in Darier's disease These occur at both follicular and nonfollicular sites In places, there may actually be horny plugs, which contain the so-called grains and corps ronds In other sites the horny plugs may be in close proximity to lacunas, and there may be cystlike spaces containing corps ronds and grains The epithelium itself (stratum granulosum and stratum spinosum) is generally thickened The usual relation of an increased stratum granulosum or its absence at sites of hyperkeratosis or parakeratosis, respectively, is found in this disease In the prickle cell layer one can see the widely publicized corps ronds and grains Above the epithelial projection, there are the spaces, or lacunas, originally described by Buzzi and Miethke,[6] which Boeck[7] stated were due to a loss of cohesion of the prickle cells, permitting the formation of spaces into which fluid may enter These spaces are of recent interest because of the discussion of Hailey and Hailey's disease (familial benign chronic pemphigus[8]) The histologic features of this disease superficially resemble those of Darier's disease, but critical examination reveals that both processes have basal cell proliferation (slight in chronic benign familial pemphigus, slight to excessive in Darier's disease) and acantholysis (extreme in the first-named disease, slight to moderate in Darier's disease) Hyperkeratosis and dyskeratosis, regularly present in Darier's disease, are absent in chronic benign familial pemphigus There is a notable disturbance in the pigmentary function of the epidermis in Darier's disease Some observers have noted an excess of pigment in the basal layer, while

6 Buzzi, F, and Miethke, F Ueber die Dariersche Dermatose, an der Hand eines selbst beobachteten Falles, Monatsh f prakt Dermat **12** 9-24, 59-71, 1891

7 Boeck, C Vier Fälle von Darierscher Krankheit, Arch f Dermat u Syph **23** 857-886, 1891

8 Hailey, H, and Hailey, H Familial Benign Chronic Pemphigus, Arch Dermat & Syph **39** 679-685 (April) 1939, South M J **33** 477-481, 1940 Sachs, W, Hyman, A B, and Gray, M B Epidermolysis Bullosa A Recently Described Variant, Arch Dermat & Syph **55** 91-100 (Jan) 1947

epidermis Corresponding to the sites of greatest hyperkeratosis, there was basal cell proliferation At one site (fig 6) was a typical lesion of Darier's disease (perifollicular) with hyperkeratosis, corps ronds, lacunas and slight basal cell proliferation There was slight round cell infiltration of the corium, and the appendages (sweat apparatus) were normal

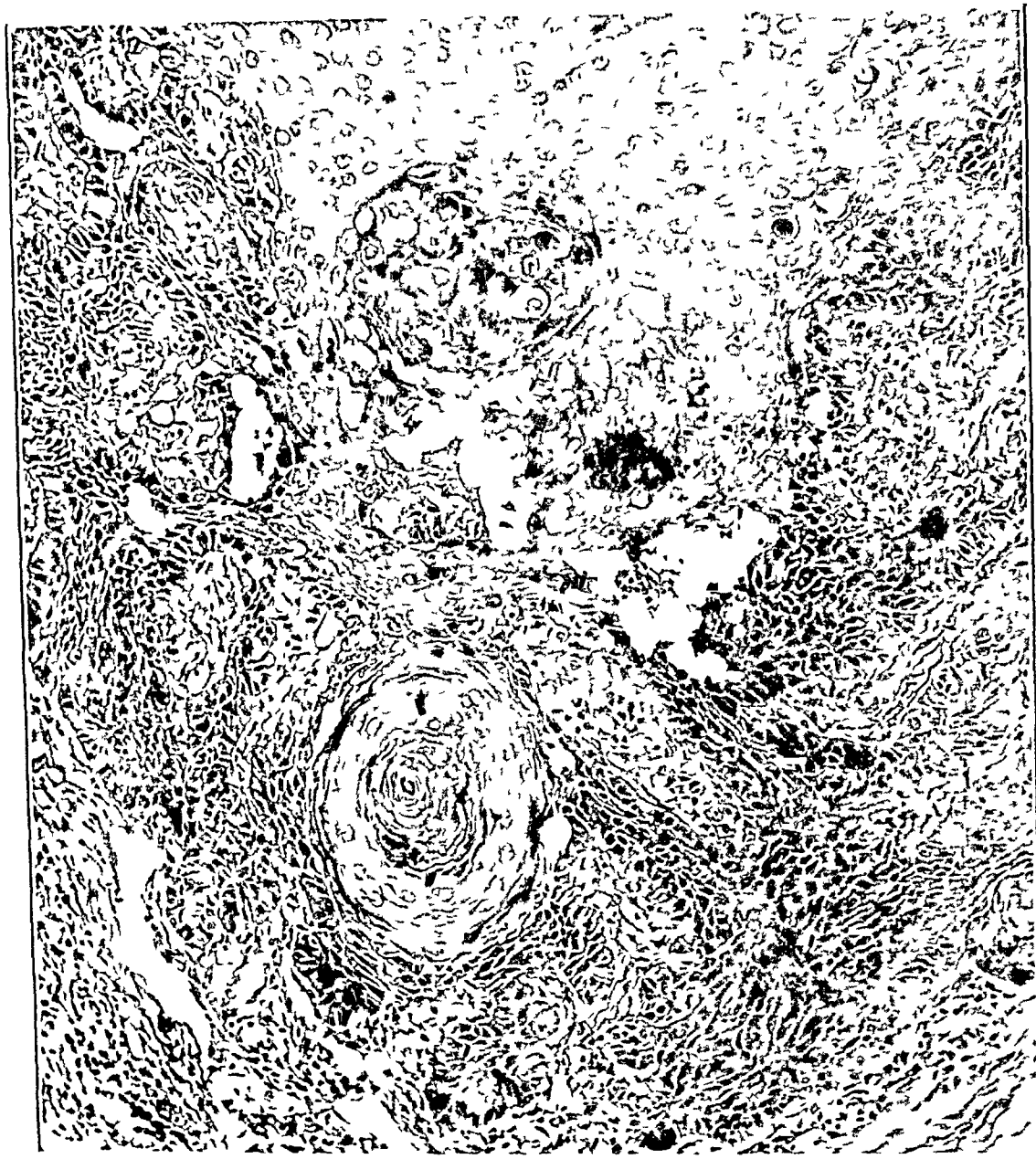


Fig 7 (case 2) —Section of a lesion from the supraorbital region In addition to the features of Darier's disease (hyperkeratosis, corps ronds and lacunas) there are distinct basal cell proliferations and pseudopearls (slide 946)

Section 946 was taken from the supraorbital region The specimen had a definitely irregular surface, pronounced cauliflowerlike hyperkeratosis, frequent keratotic follicles and a profusion of corps ronds and grains There were deep fissures, some of which extended the whole width of a rather deep section. These fissures were lined with keratin The same features were present throughout the

layer which have long been recognized in this disease and which we wish again to emphasize to American dermatologists It must be stressed at the onset that this basal cell proliferation is a feature of all cases of Darier's disease but becomes a highly distinctive and prominent characteristic of the vegetative cases The basal cell layer forming the base of the lacunas no longer presents its usually orderly arrangement but shows evidence of a change superficially resembling epithelioma There are long, small, tubelike or finger-like proliferating processes, composed of basal cells, which penetrate deep into the corium These projections send out side branches Lacunas are present among the proliferating interpapillary pegs Here and there corps ronds are discernible There may, in addition, be cells with hyalin bodies, as well as grains Frequently the thickened basal cell layer shows numerous mitotic figures Darier [15] had already called attention to this phenomenon of basal cell hyperplasia in his earliest publications He made the following statement

I should like to add a few words concerning the exuberant lesion of the inguinal region in case 2

Section of these tubercles shows, around a dilated pilosebaceous follicle, ramifying epithelial processes separated by strands of connective tissue, the whole contituting a structure like that of a papilloma or epithelioma The condition is evidently due to an exaggeration of the proliferation of the interpapillary epithelial processes, already referred to in connection with the smaller lesions The excessive proliferation explains the hypertrophic character of the lesions about the pubes and the groins of man The dilated pilosebaceous orifice is filled with sebaceous matter which contains numerous "grains" and some bacteria The epithelial vegetations contain "round bodies"

Boeck also had demonstrated the proliferation of the interpapillary pegs which split and spread below, and Jarisch and Matzenauer,[16] in 1908, mentioned proliferations of the rete malpighii, whose projections were partly in the form of a broad club or partly drawn to a fine point and pushed on deep into the corium Brunauer stated that gradually, however, in the presentations of various authors, the discussions of the pathogenesis of the corps ronds, grains, lacunas and fissures claimed more and more attention, and the phenomenal changes in the basal cell layers were forgotten or were considered of little significance A revival of interest in these observations occurred in the German and Italian

15 Darier, J, in Unna, P G, Morris, M, Duhring, L A, and Leloir, H Internationaler Atlas von seltener Hautkrankheiten, Hamburg, L Voss, 1893, pts 8 and 9

16 Jarisch, A Die Hautkrankheiten, revised by R Matzenauer, ed 2, Vienna, A Holder, 1908, p 690

pronounced basal cell proliferation and a deep crypt (large lacuna) plugged with a crust of hyperkeratotic material and corps ronds and papilliferous projections pointed into the interior The projections were covered by a single layer, or sometimes several layers, of flat to cuboidal epithelial cells There was some pigment in chromatophores in the projections Beneath this structure occurred sweat ducts such as are seen in nevus syringocystadenomatosus papilliferus The corium con-



Fig 9 (case 2) —Higher power view of the "intracystic" proliferations Note the single layer of basal cells on the projections (slide 943, × 235)

tained leukocytes, lymphocytes, plasma cells and numerous chromatophores There were dilated blood vessels Typical features of Darier's disease (lacunas, hyperkeratosis, corps ronds, pseudoepitheliomatous basal cell hyperplasia, and pseudopearls) were to be seen at the other edge of the section (figs 8 and 9)

Section 1557, removed from the right cheek, showed essentially the same features as did section 946 Conspicuous basal cell proliferation could be noted

own and others' experience in dealing with this characteristic proliferation of the basal cell layer of the skin and mucous membranes

It is somewhat surprising that the proliferation of basal cells in Darier's disease is given so little notice by American dermatologists

Since Morrow [31] in 1894 called attention to Darier's findings with regard to the vegetations in the inguinal region, which histologically resembled "an epithelioma having its origin in the follicle," few later American texts have stressed this feature of the histology of this disease Mention of it is, for example, entirely lacking in the works of Andrews,[32] Sutton and Sutton,[33] Ormsby and Montgomery [34] and Knowles, Corson and Decker [35] McCarthy,[36] on the other hand, in his volume on histopathology, made the following statement

> The epithelium as a whole appears somewhat thickened That portion of the epithelium which surrounds the horn-filled invaginations has a tendency to atypical proliferation in the form of rete cones either rounded on their ends or drawn out to a point These cones often penetrate fairly deeply into the corium and although they produce a picture very suggestive of epitheliomatous growths, no cases resulting in malignancy have been reported This finger-like proliferation of the rete cones is considered very typical of Darier's disease

Frost,[37] as well as Pinkus and Epstein,[38] also recently noted, in passing, the basal cell proliferation in Darier's disease Goodman,[38a] on the basis of his experience, stated the belief that hyperplasia of basal cells is the most prominent feature of Darier's disease

Part of the reason for this general lack of emphasis on the basal cell proliferation in American literature is probably, as Wile [39] indicated, the result of the fact that in most of the cases observed and described in this country the disease is much milder than it is in ones

31 Morrow, P A A System of Genito-Urinary Diseases, Syphilology and Dermatology, New York, D Appleton & Company, 1894, vol 3, pps 628-633

32 Andrews, G C Diseases of the Skin, ed 3, Philadelphia, W B Saunders Company, 1946

33 Sutton, R L, and Sutton, R L, Jr Diseases of the Skin, ed 10, St Louis, C V Mosby Company, 1939

34 Ormsby, O S, and Montgomery, H Diseases of the Skin, ed 6, Philadelphia, Lea & Febiger, 1943

35 Knowles, F C, Corson, E F, and Decker, H B Diseases of the Skin, ed 4, Philadelphia, Lea & Febiger, 1942

36 McCarthy, L Histopathology of Skin Diseases, St Louis, C V Mosby Company, 1931

37 Frost, K Dyskeratosis Follicularis (Darier's Disease), Arch Dermat & Syph **31** 508-511 (April) 1935

38 Pinkus, H, and Epstein, S Familial Benign Chronic Pemphigus Report of Case, Arch Dermat & Syph **53** 119-124 (Feb) 1946

38a Goodman, M H, in discussion on Frank and Rein [54]

39 Wile, U J, in discussion on Chambers, S, and Anderson, S Keratosis Follicularis (Darier), Arch Dermat & Syph **39** 358 (Feb) 1939

HYPERTROPHIC DARIER'S DISEASE

Clinical Characteristics The essential papillomatous character of hypertrophic Darier's disease, from the clinical standpoint at least, is suggested by some of the names proposed for the process, as they were collected by Brunauer [3] *acné concréte hypertrophique* (Hallopeau), *acné cornée végétante* (Gaucher), keratosis vegetans (Crocker), *séborrhéide végétante* (Hallopeau and Fouquet), epitheliomatosis miliaris (Nékám) and *papillomatose dyskératosique* (Nicolau) Although Darier [4] later (1931) concluded that the first two points of his designation for the disease were unjustifiable, he did not deny the appropriateness of the third (*végétante*)

In Darier's disease there may be a variety of types of lesions, the sort depending on the site involved The process usually has a tendency to the seborrheic distribution, with a special predilection for loci of intense perspiration These include the scalp, temples, face (cheeks and nasolabial folds), retroauricular regions, neck and axillas, the presternal, interscapular, umbilical and genitocrural regions, and the mons veneris, back, gluteal regions, legs, dorsa of the feet, soles, dorsa of the hands and palms Verruca plana may occur on the dorsa of the hands (Darier [4]) The vegetative form involves the intertriginous regions, the axillas, the inguinal and anogenital regions and, less often, the postauricular areas Hidaka [5] found that among 70 patients with Darier's disease, the axillas and inguinal region were affected 13 times each, the genitocrural region 8 times and the anal region 6 times In these sites, by confluence of individual lesions, the macerating effects of intertriginous surfaces and secondary infection contribute to the unusually large size of the lesions, as well as to the characteristic foul odor, matting and crusting Clinically, the lesions, which are reddish yellow, may be plaquelike, fungating, condylomatous, papillomatous, cockscomb-like or tumorous, and sometimes there are deep fissures Some of the lesions, umbilicated papules, may not exceed the size of a pea and morphologically resemble those of molluscum contagiosum The crater, occasionally completely empty, is usually occluded by a gray or yellow sebaceous material The size and odor of the lesions contribute greatly to the patients' depressed mental attitude toward this disease

3 Brünauer, S R, in Jadassohn, J Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol 8, pt 2

4 Darier, J, in the Proceedings of the Eighth International Congress of Dermatology, Copenhagen, Engelsen and Schrøder, 1931

5 Hidaka, S Studier über die Dariershe Dermatose, Acta Dermat **3**.191 and 373, 1924, **4** 1, 1924, abstracted, Zentralbl f Haut- u Geschlechtskr **17**.873, 874 and 875, 1925

and may be greatly increased in number, have retained for the most part the characteristics of normal epithelial cells

Pseudoepitheliomatous hyperplasia in chronic inflammation has long been difficult to differentiate from cancer of the skin More difficult of distinction is the grade 2 or 3 hyperplasia seen occasionally at the edge of chronic ulcers, but especially in verrucous lesions, as typified by bromoderma Narrow strands of epithelial cells, containing numerous mitotic figures, are seen penetrating deeply into the cutis Except for the mitosis, however, the epidermal cells contained in these strands present none of the features of malignant cells, such as changes in nucleoli and an increase in the size of the nucleus in relation to the amount of cytoplasm (MacCarty [48]) Furthermore, these narrow epithelial strands are invaded by leukocytes with apparent disintegration of some of the epidermal cells, a phenomenon which usually is not seen in the narrow strands of squamous cell epithelioma, grade three or four, though in the latter the strands may be surrounded by a dense infiltrate White and Weidman emphasized that every gradation up to perfect imitation of epithelioma may occur, so that it becomes impossible to distinguish histologically between squamous cell epithelioma and nonmalignant hyperplasia These authors stated the belief that a diagnosis of carcinoma is not justified unless the infiltration extends to the level of the sweat glands or farther or unless the pathologist has had wide acquaintance with the behavior of hyperplastic epidermis in general Winer,[49] in his review on this subject, summarized the diagnostic characters which have been reported to differentiate hyperplasia from true cutaneous carcinoma He expressed the conclusion that the most frequently noticed histologic change was edema of the upper part of the cutis and in the epidermis of all the sections which showed pseudoepitheliomatous hyperplasia The edema caused vacuolation of the intercellular spaces in the lower portion of the epidermis and disintegration and vacuolation of the epidermal cells in the upper part of the epidermis Although the edema was diffuse, the pseudoepitheliomatous proliferation was, as a rule, localized to a single area Therefore, the factor of nutrition must be considered in the search for a possible cause of the hyperplasia This epithelial change has been noted in a number of cutaneous diseases, to which Darier's disease must be added

When one makes a histologic comparison between the pseudoepitheliomatous changes in Darier's disease and those in epithelioma, one

48 MacCarty, W C Identification of the Cancer Cell, J A M A **107** 844-845 (Sept 12) 1936

49 Winer, L H Pseudoepitheliomatous Hyperplasia, Arch Dermat & Syph **42** 856-867 (Nov) 1940

others (Hidaka) have observed a diminution or absence of pigment (Mu[9]) In one of the sections (1988) from the second patient with Darier's disease mentioned in this paper, there was evidence of metaplasia of the basal cells into prickle cells, the latter cells occurring at a site where basal cells should have occurred The significance of this observation is uncertain, but the change has not been previously noted As a rule metaplasia is infrequently recorded in dermatopathology, but Weidman[10] mentioned it in connection with the epithelial cells lining the sweat ducts in the presence of surrounding acute inflammatory processes attended by, or near, suppuration Walther and Montgomery[11] found metaplasia in the direction of mucinous glands in the cells of the epidermis that had begun to differentiate toward sweat ducts Stokes[12] also noted metaplasia of epithelium lining the ducts of the sweat apparatus near the cutaneous surface in his case of nevus syringocystadenomatosus papilliferus The papillae are lengthened, shortened, hardened and flattened In case of widespread lesions the papillae may be atrophic in the centers of the lesions and elongated at the periphery, this distribution yielding a microscopic picture of a central dell In the corium one finds perivascular infiltration, chiefly with lymphocytes, and a scattering of plasma, mast cells and leukocytes, including eosinophils Melczer[13] was able to demonstrate, in a case of vegetative Darier's disease, masses of plasma cells, as well as intracellular fuchsinophilic bodies, around the epithelioma-like epithelial proliferation Changes similar to those on the cutaneous surfaces have been noted in the lesions of the mucous membrane The details of the various changes have been thoroughly collated by Brunauer and by Miani[14]

Of particular interest to me and to my associates, because of the papillomatous cases here presented, are the relations of the basal cell

9 Mu, J W Beitrag zur Untersuchung der Pigmentverhaltnisse beim Morbus Darier, Acta dermat-venereol **11** 365-372, 1930

10 Weidman, F D The Border Zone Between the Hyperplastic and Neoplastic Processes of Cutaneous Epithelium, Am J M Sc **165** 479-485, 1928, Metaplasia (Acute) of Sweat Duct Epithelium in Acute Suppurations, Arch Dermat & Syph **10** 275-278 (Sept) 1924

11 Walther, M, and Montgomery, H Schweissdrusentumor mit Epithelmetaplasie, Arch f Dermat u Syph **163** 420-426, 1931

12 Stokes, J H A Clinico-Pathologic Study of an Unusual Cutaneous Neoplasm Combining Naevus Syringadenomatosus Papilliferus and a Granuloma, J Cutan Dis **35** 411-425, 1917

13 Melczer, N Zur Histologie der sogenannten Darierschen Dyskeratose (Epitheliomatosis miliaris Nekam), Dermat Wchnschr **83** 1127-1136, 1926

14 Miani, G La malattia di Darier allo stato attuale delle nostre conoscenze, Arch ital di dermat, sif **15** 433-510, 1939

follicular The response or lack of response of Darier's disease to vitamin A therapy, noted by a host of recent writers (Jeghers,[58] Peck and associates,[59] Carleton and Steven [60] and Pettler [61]) does not argue for or against the follicular character of the dermatosis The patient of the second case described herein received massive doses of vitamin A without material benefit A strong argument against the follicular nature of Darier's disease is the occurrence of lesions on the mucous membranes, where hair follicles do not usually exist (Kren,[62] Spitzer,[63] and Brunauer) One is mindful of the ever present possibility of aberrant hair follicles, analogous to the sebaceous glands found on the mucous membrane in Fordyce's disease

Similarly, there is practically no evidence that Darier's disease is a lesion of the sweat glands, although there have been a number of investigators who have supported this idea (Wende, Ormerod and MacLeod,[64] Jordan,[65] Bukovsky,[66] Buzzi and Miethke and C Boeck) Hidaka showed, however, that in 121 of 163 lesions (74 2 per cent) there was no relation, in 36 lesions (23 9 per cent) there was close proximity to sweat apparatus and in 3 cases there were sweat glands opening in the center of the lesion, though there was no hyperkeratosis in these glands In a process as extensive as those in our cases, it is hardly likely that many lesions could escape being close to sweat apparatus This fact does not, however, indicate that the sweat apparatus was necessarily participating in the changes My associates and my failure to demonstrate myoepithelium in the finger-like processes projecting into the lacunas is only negative evidence against origin from the sweat glands, since in undoubted lesions of the sweat glands the myoepithelium may be absent

58 Jeghers, H Skin Changes of Nutritional Origin, New England J Med **228** 678-686 and 714-723, 1943

59 Peck, S M , Chargin, L , and Sobotka, H Keratosis Follicularis (Darier's Disease) A Vitamin A Deficiency Disease, Arch Dermat & Syph **43** 223-229 (Feb) 1941

60 Carleton, A , and Steven, D M Keratosis Follicularis A Study of Four Cases, Arch Dermat & Syph **48** 142-150 (Aug) 1943

61 Pettler, M F The Effect of Vitamin A in Pityriasis Rubra Pilaris and Keratosis Follicularis, Pennsylvania M J **45** 604-605, 1942

62 Kren, cited by Brünauer [3]

63 Spitzer, R Zur Kenntnis der Darierschen Krankheit, Arch f Dermat u Syph **135** 362-376, 1921

64 Ormerod, J A , and MacLeod, J M H On a Case of Darier's Disease, Brit J Dermat **16** 321-334, 1904

65 Jordan, A Fall von Darier, abstracted, Dermat Wchnschr **58** 150, 1914, Die Dariersche Krankheit, ibid **73** 889-900, 1921

66 Bukovsky, J Psorospermosis follicularis vegetans Darier, Arch f Dermat u Syph **75** 279-302, 1905

literature (Fasal,[17] Kreibich,[18] Ravogli,[19] Sachs[20] and Nékám[21]) Bellini,[22] for example, spoke of new formations of tubules and cords of epithelial formation derived from the basal cell layer Bizzozero[23] mentioned the numerous mitotic figures in the basal cell layer below the lacunas, as well as epithelial proliferation into the connective tissue at these sites Martinotti[24] also referred to the basal cell hyperplasia, which approached a neoplasm of basal cells, and the transformation of keratinization The whole subject was thoroughly reviewed by Pinkus and Ledermann in 1921[25] on the basis of a case, presumably the most extreme to that time, but apparently from their data much milder than either of our cases In addition to hyperkeratosis, dyskeratosis, broadening of the papillae and changes in the cutis, these authors noted the change in the epithelium surrounding the hair follicle The epithelium sends out processes resembling epithelioma, with lumens in their depths The cells of these tubelike projections are cuboidal epithelial cells These processes are at the bottom of the grotesque, luxuriant, papillary growth Zieler and Jacobi,[26] as well as Frieboes,[27] Hamdi,[28] Kyrle[29] and Gans,[30] described similar changes in the descriptions of Darier's disease in their texts Parallel with the changes in the skin, a similar phenomenon occurs in the mucous membranes in Darier's disease Brunauer, in his monograph, reviewed his

17 Fasal, H Ein Fall von Darierscher Krankheit, Arch f Dermat u Syph **74**·13-22, 1905

18 Kreibich, K Zum Wesen der Psorospermosis Darier, Arch f Dermat u Syph **80** 367-378, 1906

19 Ravogli, A Psorospermosis cutis, Monatsh f prakt Dermat **18**:165-177, 1894, **19** 81, 1894

20 Sachs, O Psorospermosis follicularis Darier, Wien med Wchnschr **56**.457-462 and 570-575, 1906

21 Nékám, cited by Melczer[10]

22 Bellini, A Discheratoma nevico (psorospermosi follicolare vegetante di Darier), Gior ital d mal ven **55**.776-823, 1914

23 Bizzozero, E Ueber die Dariersche Dermatose, Arch f Dermat u Syph **93**:73-84, 1908

24 Martinotti, cited by Brünauer[3]

25 Pinkus, F, and Ledermann, R Beitrag zur Histologie und Pathogenese der Darierschen Krankheit, Arch f Dermat u Syph **131** 360-377, 1921

26 Zieler, K W F, and Jacobi, E Lehrbuch und Atlas der Haut- und Geschlechtskrankheiten fur praktische Aerzte und Studierende, Vienna, Urban & Schwarzenberg, 1924

27 Frieboes, W Grundriss der Histopathologie der Hautkrankheiten, Leipzig, F C W Vogel, 1921

28 Hamdi, H Morbus Darier, Virchows Arch f path Anat **279**.237-243, 1930

29 Kyrle, J Vorlesungen über Histobiologie der menschlichen Haut und ihrer Erkrankungen, Berlin, Julius Springer, 1925

30 Gans, O Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925

The favorite sites are the shoulders, the axillae, the genito-inguinal and surrounding regions and the hairy portion of the scalp The lesions are rose-red papules of firm consistency from the size of a millet seed to that of a hemp seed, usually arranged in groups Owing to their transparent nature, one or more vesicle-like inclusions may often be distinguished, these inclusions are from the size of a pin-point to that of a pin-head and filled with clear fluid In addition, the papules are umbilicated at their summit, being similar to lesions of molluscum contagiosum (Because of this finding, solitary lesions of long duration clinically resembling lesions of molluscum contagiosum may prove to be nevi of the type under consideration) The papules stand out discretely or form directly confluent plaques In one case (Kreibich [70]) papillary growths were observed on the surface of such a plaque

Elliot [71] in 1893 described a linear (systematized) lesion Occasionally the lesion may become malignant (Horn [72])

Not infrequently the tumor extends through the whole thickness of the corium, rarely it arises near the epidermis The sweat glands are somewhat dilated and the sweat ducts cystic in places The inner surface of the cavity of the duct contains small, villus-like projections The lining is composed of two or more layers of cells, including an outer columnar and inner cuboidal layer The epidermis is acanthotic, there may or may not be an associated inflammatory reaction Stokes reported a reaction suggestive of granuloma pyogenicum or vegetative dermatitis with plasma cells The nature of the lesion is not definitely known, and it has been considered congenital by some Other associated cutaneous lesions of an inflammatory nature have suggested a reactive process

Stokes reported the first American case under the title of nevus syringadenomatosus papilliferus Comprehensive reviews (Nodl,[73] Sachs and Lewis, Mayer,[74] Reuterwall,[75] Plantevin [76] and Biberstein [77]) of this subject are based on relatively few cases My associates and I

70 Kreibich, cited by Frieboes,[27] p 186

71 Elliot, G T Adeno-Cystoma Intracanaliculare Occurring in a Naevus Unius Lateris, J Cutan Dis **11** 168-173, 1893

72 Horn, R C, Jr Malignant Papillary Cystadenoma of Sweat Glands with Metastases to the Regional Lymph Nodes, Surgery **16** 348-355, 1944

73 Nodl, F Beitrag zum Naevus syringo-cystadenomatosus papilliferus, Arch f Dermat u Syph **178** 697-713, 1939

74 Mayer, I Zur Histologie der Hidroadenome, Frankfurt Ztschr f Path **55** 548-590, 1941

75 Reuterwall, O Naevus Syringo-Cystadenomatosus Papilliferus and Its Relation to Malignancy, Acta path et microbiol Scandinav, 1933, supp 16, pp 376-387

76 Plantevin, P L'hidradenome verruqueux fistulo-vegetant Etude des malformations et etats precancereux de la peau, Thesis, Paris, Amedee Le Grand, 1927

77 Biberstein, H Ueber papilliforme Syringocystadenome, Arch f Dermat u Syph **152** 602-610, 1926

seen abroad A survey of the cases of Darier's disease presented in the various local and national dermatologic societies in America, as reported in the ARCHIVES (1920-1946), reveals that about 10 of 120 cases reported showed papillomatous lesions There was no mention of the pseudoepitheliomatous change in the histologic reports of any of these cases On the other hand, although 2 of 9 cases of Darier's disease reported at the Copenhagen Congress of Dermatology and Syphilology in 1930 were of the vegetative type, this form is now rated as being of rare occurrence even in France (Perin [40])

Although dysplasia of basal cells and proliferation of epithelioma-like proportions histologically occur in Darier's disease, no really authentic case of secondary development of carcinoma has been reported Wende's [41] patient obviously had multiple epitheliomatosis, probably of arsenical origin (Montgomery [42]) Charache's [43] case likewise, although studied by a competent general pathologist, was not documented by histologic illustrations A small lymph node was excised from the inguinal region, and concerning the specimen it was simply stated that a diagnosis was made of Darier's disease with malignant transformation Occurrence of Darier's disease associated with epithelioma of the nose, reported by Wise and Parkhurst [44] and by Streitmann,[45] represents coincidental, and not related, processes

We believe that the basal cell changes in Darier's disease do not differ essentially from the now widely recognized epithelial response to a stimulus, which response is variously known as benign penetrating epithelium (Broders [46]) or pseudoepitheliomatous hyperplasia (White and Weidman [47]) The epithelial cells in this state, although they may penetrate far beyond the normal level of the dermoepidermal junction

40 Perin, L Maladie de Darier, in Darier, J, and others Nouvelle pratique dermatologique, Paris, Masson et Cie, 1936, p 392

41 Wende, G W Keratosis Follicularis Resulting in Multiple Epithelioma Report of a Case, J Cutan Dis **26** 531-551, 1908

42 Montgomery, H Arsenic as an Etiologic Agent in Certain Types of Epithelioma Differential Diagnosis from, and Further Studies Regarding, Superficial Epitheliomatosis and Bowen's Disease, Arch Dermat & Syph **32** 218-236 (Aug) 1935

43 Charache, H Darier's Disease with Malignant Transformation, Arch Dermat & Syph **35** 480-484 (March) 1937

44 Wise, F, and Parkhurst, H J Notes on Two Unusual Cases of Darier's Disease, Arch Dermat & Syph **2** 430 (Oct) 1920

45 Streitmann, Morbus Darier, Zentralbl f Haut- u Geschlechtskr **55** 616, 1937

46 Broders, A C Carcinoma in Situ Contrasted with Benign Penetrating Epithelium, J A M A **99** 1670-1674 (Nov 12) 1932

47 White, C, and Weidman, F D Pseudo-Epitheliomatous Hyperplasia at the Margins of Cutaneous Ulcers, with Especial Reference to Histologic Diagnosis, J A M A **88** 1959-1963 (June 18) 1927

have encountered but 1 example among 3,000 specimens for biopsy taken from cutaneous lesions and submitted to our laboratory

CASE 3.—L. N., a white deaf-mute aged 20, on Nov. 2, 1931, presented above his right ear a sharply localized granulomatous lesion with eroded top, irregular in outline and associated with several flat-topped satellite lesions. This process had begun when the patient was 1 year old, and it had not grown much in size. The clinical diagnosis was granuloma, but histologically the lesion showed typical

Histologic Comparison of Darier's Disease and Nevus Syringocystadenomatosus Papilliferus

	Darier's Disease	Nevus Syringocystadenomatosus Papilliferus
Hyperkeratosis	Massive	Usually absent
Parakeratosis	May be extreme in places	Usually absent
Dyskeratosis Corps ronds Grains	Present	Absent
Lacunas	Characteristic	Absent
Basal cell proliferation	Constant, round lacunas in papillomatous cases, extreme pseudoepitheliomatous change involving prickle cell metaplasia	Rare indeed, when present suggests epithelioma of basal cells
Papillary excrescences	Short, compact, and involved, project into lacunas, covered with one or more cell layers	Variously long and dendritic, may project on surface or into cysts, may be on remnants of walls of confluent cysts, covered with only two layers of cells
Relation to appendages and sweat apparatus	Questionable	Essential part, may be intracanalicular proliferations of epithelium of cystic duct (not apocrine glands)
Relation to pilosebaceous apparatus	Present in some cases	None
Pigmentation	Disturbance in epidermal pigmentary function early, stimulation and proliferation, later, feeble, more pronounced near edges of epidermal overgrowths	May be present in chromatophores near the edge of the lesion
Location	Superficial in the usual case, deep in papillomatous cases	Both superficial and deep in cutis
Cyst contents	No cysts	Cellular detritus
Cyst opening		Bottle like, narrow neck
Myoepithelium	None	Sometimes present
Malignant change	Rare, if ever	Occasional
Plasma cells	May be present	May be present

features of nevus syringocystadenomatosus papilliferus (see figs. 11 and 12). Recurrence after removal occurred within fourteen years (December 1945).

While the nature of this usually benign tumor is not clear, most authorities have agreed that it is derived from the sweat apparatus (Dorffel[78]). Gates, Warren and Warvi[79] made the claim that the

78. Dorffel, J.: Naevus syringo-cystadenomatosus papilliferus, Dermat. Wchnschr. **99**: 1318-1324, 1934; Zur Histogenese des Naevus syringo-cystadenomatosus papilliferus, ibid. **100**: 229-231, 1935.

79. Gates, O., Warren, S., and Warvi, W. N.: Tumors of Sweat Glands, Am. J. Path. **19**: 591-631, 1943.

notes that there are a number of similarities Both may contain basal cell proliferation, both, as well as other diseases (Meierowsky [50]), may contain dyskeratotic cells, and both may contain fissures and lacunas

Although Darier's disease has been known to occur or become aggravated after acute infections and other irritative processes, such as furunculosis, croup, erysipelas, variola, vaccination, ptomaine poisoning and sunlight (Preissmann [51]), these disorders can hardly be the basis for the long-continued, intermittent course of the process The presence of the Koebner phenomenon in Darier's disease, as demonstrated by Bettmann,[52] suggests that there may still be a fundamental relation between Hailey and Hailey's [8] disease (Pels and Goodman [53]) and Darier's disease, since Frank and Rein [54] found a definite response to trauma in the cases which they studied

In the interpretation of the histologic features of Darier's disease, the relation of the process to the cutaneous appendages (sweat and pilosebaceous) is of importance At times one finds lesions of this disease in the proximity of, or actually surrounding, a hair follicle This fact undoubtedly originally led Darier,[55] as well as White,[56] to the idea that the process was follicular Numerous others have shown the lesions to be extrafollicular (observations collected by Miami and by Brunauer) For example, Ellis,[57] in his review, expressed the opinion that Darier's disease is a benign dyskeratosis, which incidentally affects the hair follicles Hidaka, who also found no relation of the lesions to the hair follicle in the majority of the cases, showed that 112 of 163 lesions (68 6 per cent) were nonfollicular, 50 lesions (30 7 per cent) were near follicles, and only 1 lesion was actually peri-

50 Meierowsky, E The Paget Cell Its Structure, Occurrence and Significance, Proc Roy Soc Med **38** 495-499, 1945

51 Preissmann, M De l'action provocatrice de la lumière dans la maladie de Darier Étude histologique des efflorescences provoquées expérimentalement en peau saine par les rayons ultra-violets, Ann de dermat et syph **6** 188-203, 1946

52 Bettmann Ueber Umbauvorgange als Ausdruck spezifischer Reaktionsfahigkeit bei Hautkrankheiten (Die Reizbarkeit der Haut bei der Darierschen Krankheit), Arch f Dermat u Syph **135** 65-76, 1921

53 Pels, I R, and Goodman, M H , Criteria for the Histologic Diagnosis of Keratosis Follicularis (Darier) Report of a Case with Vesiculation, Arch Dermat & Syph **39** 438-455 (March) 1939

54 Frank, S B, and Rein, C R Dyskeratoid Dermatosis, Arch Dermat & Syph **45** 129-151 (Jan) 1942

55 Darier, J De la psorospermose folliculaire vegétante, Ann de dermat et syph **10** 597-612, 1889

56 White, J C A Case of Keratosis (Ichthyosis) Follicularis, J Cutan & Genito-Urin Dis **7** 201-209, 1889

57 Ellis, F A Keratosis Follicularis Is Not Primarily a Follicular Disease, Arch Dermat & Syph **50** 27-30 (July) 1944

ABSTRACT OF DISCUSSION

DR. FRANCIS A ELLIS, Baltimore Since I was one of the dissenters from the diagnosis of hypertrophic Darier's disease in case 1 when it was presented in 1940, Dr Weidman permitted me to have a section for study

The slide was shown several times to the Baltimore group of dermatologists and sent to five nationally known dermatohistopathologists Dr Hermann Pinkus was the only one who made the diagnosis without the aid of the clinical history His father, Dr Felix Pinkus, had previously reported a similar case

Dr Beerman also sent us sections from his second case It was the extreme pseudoepitheliomatus hyperplasia and the proliferation of the basal layer, forming acini and villi, which suggested the diagnosis of nevus syringocystadenomatosus papilliferus, but finally, after more careful studies had been made, it was these same features which confirmed the diagnosis of hypertrophic Darier's disease

It should be emphasized that the cells lining the acini in hypertrophic Darier's disease are usually composed of a single layer of cells resembling basal cells, but, in the nevus of the sweat glands, there are two rows of cells, such as are seen in an apocrine sweat gland

In studies of the so-called bullous Darier's disease, emphasized by Pels and Goodman and Hailey and Hailey, this feature of the formation of acini covered by one layer of cells resembling basal cells was also found The acini or villi will be present in the dry or vesicular form if the three following features are present proliferation of the basal layer, formation of lacunas and the more extreme stages of acanthosis (hypertrophy)

The presence of these features in the vesicular type has not been stressed previously, but they were observed in about half of the biopsies made by my associates and me and were especially prominent in a specimen taken from a patient who had hypertrophic lesions in the groin

Again it should be emphasized that in the vesicular type the pathologic changes are usually not follicular but tend to miss the follicles, that is, they approach the neck of the adnexa and then stop The moist type is therefore similar in these two respects to the dry form but differs histologically in the lack of dyskeratosis and the associated alterations

We have never observed histologically in epidermolysis bullosa the typical lacunas which are found in the bullous form of Darier's disease

I wish that Dr Beerman would discuss in more detail why lacunas occur Can the rete cells rejoin so that one at times can see a fairly normal epidermis above the lacunas? The degree of unalteration in the rete layer above the lacunas is one of the striking differential features between the two types, the bullous form tends to have a more normal intact prickle cell layer

DR. C GUY LANE, Boston Just a short time ago I saw at one of the state hospitals in Massachusetts a patient whose case fits into the picture of hypertrophic Darier's disease This woman, who was 74 years old, was the oldest patient with Darier's disease that I have seen She had had Darier's disease all her life, and her father also had had the same diagnosis Earlier, she had been sent into another state hospital—a hospital for patients with cancer—because of growths in various places on her skin The principal lesion was an oval, moist, papillary lesion, 5 0 by 2 5 cm in area, in her right groin She had several other hyperkeratotic lesions on the lower part of her back and on the pubic region, as well as many follicular hyperkeratotic lesions of the face, ears and upper portion of the trunk There was some enlargement of the ears, and there was also a pronounced cutis verticis gyrata of her forehead

It is logical to assume for Darier's disease, on the question of whether the process originates from the surface or from a sweat gland or hair follicle, the same reasoning proposed by Weidman [67] to explain the occurrence in the same person of epithelial tumors apparently arising from all three, this theory is, namely, that all are derived from the same embryonic source, which is at first neither sweat duct, epidermis nor hair follicle If the potentialities for formation of a tumor in one of these embryonic sources which has remained undifferentiated develop into sudoriferous or pilary structure, the Krompecher tumor will appear, if the tumor occurs at a later time in the development of the source, a tumor of the sweat glands may result, or, if development occurs when the hair follicle is developing, a tumor of the hair follicle will be expected If the lesion occurs at the time of full differentiation, all three types of involvement may be present in the same lesion (multicentric) In the application of this explanation of the various types of involvement in Darier's disease, it is assumed that one is dealing with a nevic state, as many have maintained

DIFFERENTIATION FROM NEVUS OF SWEAT GLANDS

Only occasionally is Darier's disease mistaken clinically for a systematized verrucous nevus In such cases histologic study should afford the means of final differentiation, but, as was previously noted, a lesion of the sweat glands (nevus syringocystadenomatosus papilliferus) was considered by some for a while to be the correct histologic interpretation of 1 of our cases We believe this interpretation to be incorrect, on both clinical and histologic grounds

In the general literature of tumors, the name for a papillary growth of variable structure and uncertain nosology is hidradenoma papilliferum In dermatologic literature, however, this type of lesion is known either as nevus syringadenomatosus papilliferus (Werther [68]) or as nevus syringocystadenomatosus papilliferus, a designation for which there are no clearcut grounds (Caro [68a]) This usually solitary and slowly growing tumor occurs on the genitalia, perineum, thighs and face and scalp (sites of predilection of Darier's disease) The clinical characteristics of the process are well described by Frieboes, as cited by Sachs and Lewis [69]

67 Weidman, F D, in discussion on Stillians, A W Nevo-Epithelioma Adenoides (Cylindroma) of the Scalp, Arch Dermat & Syph **27** 481-489 (March) 1933

68 Werther, L Syringadenoma papilliferum (Naevus syringadenomatosus papilliferus), Arch Dermat u Syph **116** 865-870, 1913

68a Caro, M R Personal communication to the author

69 Sachs, W, and Lewis, G M Naevus Syringadenomatosus Papilliferus (Werther) Report of Five Cases, Arch Dermat & Syph **36** 1202-1209 (Dec) 1937

ESSENTIAL HIRSUTISM

Dermatologic and Endocrinologic Considerations

J LAMAR CALLAWAY, M D

JAMES T WORTHAM, M D

E C HAMBLEN, M D

AND

A A SALMON, B S

DURHAM, N C

HIRSUTISM in women is common Most hirsute patients come to the physician because of vanity, complaining of the cosmetic inelegance of excessive hair The psychic trauma of hirsutism, particularly when the condition involves the face, is striking Even the bearded lady of the sideshow is often miserable, despite her superficial attitude of amusement

It is because of this psychic trauma, the cosmetic appearance and the many misconceptions of the role of the endocrine glands in the development of hirsutism that we have evaluated our material It is hoped that these data may somewhat clarify the problem

To understand better abnormal hair growth, one should know normal hair growth Bissell and Williams [1] discussed hirsutism in women, and Danforth [2] recently reviewed the physiology of human hair

Before discussing normal and abnormal hair growth of the human being, we shall review the results of some animal experiments Undernourished normal rats had delayed growth of hair, although skeletal growth continued [3] On the other hand, well fed adrenalectomized rats [4]

From the Division of Dermatology and Syphilology and the Division of Endocrinology, Duke University School of Medicine and Duke Hospital

Read before the Section on Dermatology and Syphilology at the Ninety-Seventh Annual Session of the American Medical Association, Chicago, June 25, 1948

1 Bissell, G W, and Williams, R H Hirsutism in Females A Clinical Study of Its Etiology, Course and Treatment, Ann Int Med **22** 773 (June) 1945

2 Danforth, C H Physiology of Human Hair, Physiol Rev **19** 94 (Jan) 1939

3 Butcher, E O Hair-Growth in Young Albino Rats in Relation to Body Size and Quantity of Food, J Nutrition **17** 151 (Feb) 1939

4 Butcher, E O Hair Growth in Adrenalectomized and Adrenalectomized Thyerin Treated Rats, Am J Physiol **120** 427 (Nov) 1937

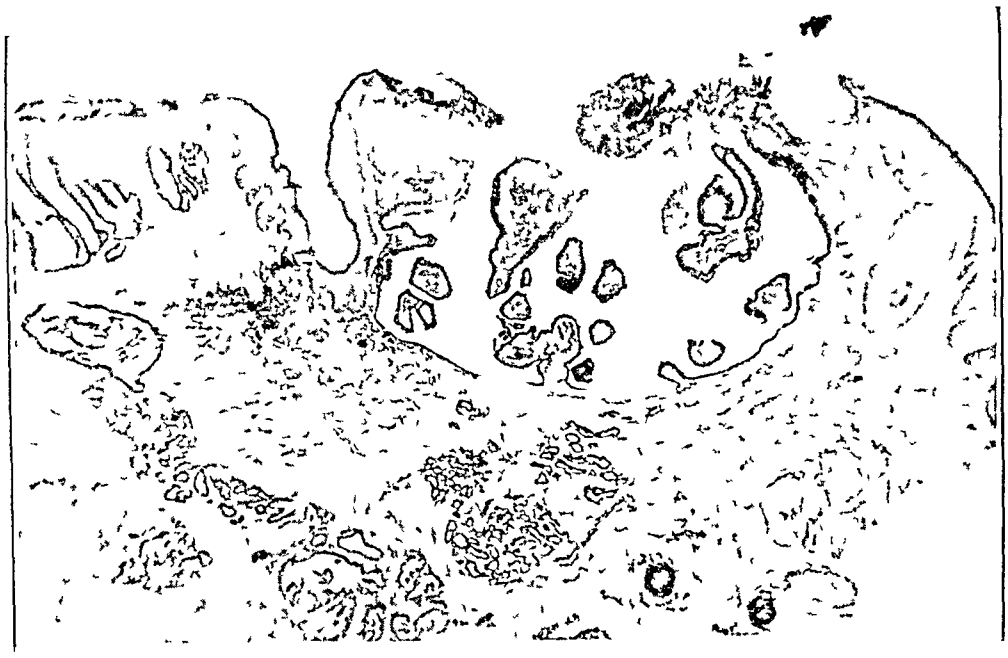


Fig 11 (case 3) —Nevus syringocystadenomatosus papilliferus Note relation to sweat apparatus and intraductal epithelial proliferation in addition to the large cyst opening to the surface, compare with fig 8 (slide 63, × 16)



Fig 12 (case 3) —Higher power view of "intracystic" projections Note double layer of epithelial cells inner, cuboidal, and outer, columnar (slide 63, × 235)

Hamilton [9] described a masculine trait which distinguishes absolutely between normal men and women This character is the growth of terminal (coarse) hairs on the external ear Three factors control development of this trait aging, endocrine stimulation (apparently androgenic) and gonadal predisposition Large auricular hairs grow in Caucasian men after the twenty-fourth year and increase in frequency and coarsen until about the fifty-fifth year, 75 per cent of the men studied exhibited this character Terminal hairs were not observed in a series of 105 women and 50 eunuchs Auricular hair appeared in 3 of 5 eunuchs receiving androgenic treatment and in 3 of 5 women with pronounced virilism Pronounced hairiness depends on age and inheritance more than on any degree of androgenic stimulation Titers of urinary steroids in 57 normal Caucasian men bore no quantitative relation to the amount of auricular hair

The endocrine glands which are chiefly concerned with hair production are the adrenal glands (cortex), the gonads, the thyroid and the anterior lobe of the pituitary [10] Prepuberal castration does not affect the appearance of ambosexual hair Since androgen therapy increases the size and number of pubic sebaceous glands of prepuberal boys, there apparently exists a synergism between the gonads and the adrenals in ambosexual hair growth in males [11] Means [12] stated that ambosexual hair of both sexes and the beard of males are diminished or absent in myxedema This may be due to the lowered metabolism, which may affect not only growth of individual hair follicles but also the functions of related endocrine glands The persistence of axillary and pubic hair after the menopause indicates the absence of any correlated ovarian influences Prepuberal ovariectomy results in the nonappearance of axillary and gynecoid pubic hair An ultimate hyperfunction of the pituitary and sequential adrenal hyperactivity, however, may be followed by growth of axillary and android pubic hair Prepubescent females with Addison's disease who have adequate function of the ovaries and of the anterior lobe of the pituitary function or females with panhypopituitarism do not have pubic or axillary hair

9 Hamilton, J B A Secondary Sexual Character That Develops in an Organ Common to Both Sexes, but Normally Only in Men, with a Discussion of the Relation of this Character to Endocrine Stimulation, J Clin Endocrinol 7 465 (June) 1947

10 Albright, F , Smith, P H , and Frasier, R. Syndrome Characterized by Primary Ovarian Insufficiency and Decreased Stature Report of Eleven Cases with Digression on Hormonal Control of Axillary and Pubic Hair, Am J M Sc 204 625 (Nov) 1942

11 Rony, H R , and Zakon, S J Effects of Androgen on the Sebaceous Glands of Human Skin, Arch Dermat & Syph 48 601 (Dec) 1943

12 Means, J H The Thyroid and Its Diseases, Philadelphia, J B Lippincott Company, 1937

epithelium is not characteristic of either the gland or the duct A reason may be that the lesion is composed of embryonal sweat apparatus (Plantevin) Biberstein could not find the iron that would be expected in the tissue if the lesion were composed of apocrine glands Because a number of reports have stressed the presence of myoepithelium in sweat gland tumors (Mayer, Sheldon[80] and Way and Memmesheimer[81]), I have hoped that demonstration of these characteristic cells might be a definitive means of differentiation between hypertrophic Darier's disease and tumors of the sweat gland Efforts in this direction have failed, a fact which Gates and her colleagues stated was probably not significant A comparison of the histologic changes occurring in this process and in Darier's disease is given in the accompanying table

SUMMARY

1 Because of the need for histologic differentiation of hypertrophic Darier's disease from nevus syringocystadenomatosus papilliferus, a review is made of the basic histologic features of Darier's disease, especially of the papillomatous form, and criteria are suggested for the histologic separation of the two processes

2 From the clinical standpoint there is little difficulty in distinguishing hypertrophic Darier's disease from nevus syringocystadenomatosus papilliferus, since the former is a disease of wide distribution and is composed of characteristic lesions The latter has usually a single lesion or a single group of lesions, likewise of fairly characteristic type.

3 Histologically, Darier's disease is essentially an epithelial process and shows peculiar cell degenerations (dyskeratoses), corps ronds and grains, hyperkeratosis and parakeratosis, acanthosis, lacunas and spaces in the epidermis and, especially in the hypertrophic form, a pronounced basal cell hyperplasia It is this last feature which has led to the histologic diagnosis of carcinoma in a specimen from a patient with a disease which rarely, if ever, becomes malignant

4 Nevus syringocystadenomatosus papilliferus shows little, if any, hyperkeratosis and parakeratosis, dyskeratosis, lacunas and basal cell proliferation On the other hand, it is a lesion of the sweat apparatus and shows regularly intracystic papilliferous projections, which are covered with two layers of cells, the outer, columnar, and the inner, cuboidal

University of Pennsylvania School of Medicine

80 Sheldon, W H The Myoepithelium in Sweat Gland Tumors Distribution, Histology, Embryology and Function, Arch Path **31** 326-337 (March) 1941

81 Way, S C, and Memmesheimer, A The Sudoriparous Glands I The Eccrine Glands, Arch Dermat & Syph **34**·797-808 (Nov) 1936

Various drugs, such as diphenylhydantoin sodium (dilantin sodium®),[17] have been reputed to cause hirsutism Permanent or transient hirsutism may accompany the menarche, pregnancy or menopause Heredity may be a factor in excessive hair growth Some families, notably Jewish and Italian ones, are hirsute The endocrine puzzle of heterosexual hirsutism was discussed in a recent editorial[18] Bissell and Williams[1] published a detailed review of the endocrine factors of normal and abnormal hair growth

We studied a group of patients with essential, or simple, hirsutism and contrasted them with patients having known endocrine disorders in order to determine whether there were any significant endocrinologic factors which could be correlated with this cutaneous manifestation Patients were not selected except for comparable laboratory and clinical data The hirsutism of the group with the essential type was severe enough to require shaving or to cause psychic disturbances, such as an inferiority complex, depression, psychoneurosis and contemplated suicide Danforth[19] stated that approximately one third of apparently normal white women have some degree of hypertrichosis

LABORATORY METHODS

Quantitative determinations of urinary gonadotropins and 17-ketosteroids were made.

Gonadotropins—Gonadotropin determinations were made on four to six consecutive twenty-four hour collections of urine Urinary extractions and bioassays were made by a method developed by one of us (A A S) in the endocrinology laboratory of Duke Hospital The procedure begins with immediate urinary dialysis, followed by complete precipitation with 95 per cent alcohol under refrigerated conditions, with the temperature lower than 10 C After the supernatant fluid has been siphoned off, the precipitate is washed several times with acetone and ether and dried under a vacuum An aqueous elution of the dried powder is injected subcutaneously into immature female albino rats The assay units are based on fractional, twenty-four hour urinary aliquots, which cause a minimal increase of 100 per cent in uterine and ovarian weights over those of control rats given injections of known negative extracts Values for normally menstruating female adults, exclusive of preovulatory wave, are as follows 3 to 10 rat uterine units per twenty-four hours, with an average of 5 units, and 1 5 to 5 rat ovarian units per twenty-four hours, with an average of 3 units

17 Goodman, M A, and Gilman, A The Pharmacological Basis of Therapeutics, New York, The Macmillan Company, 1941 Palmer, H D, and DeRonde, M Reversible Testosterone Induced Virilism, J Clin Endocrinol **3** 428 (July) 1943

18 The Endocrine Puzzle of Heterosexual Hypertrichosis (Hirsutism), editorial, J Clin Endocrinol **3** 426 (July) 1943

19 Danforth, C H Studies on Hair, with Special Reference to Hypertrichosis, Arch Dermat & Syph **11** 494 (April), 637 (May), 804 (June) 1925, **12** 76 (July), 195 (Aug), 380 (Sept), 528 (Oct) 1925

DR FRED D WEIDMAN, Philadelphia Dr Beerman has brought us a number of messages One is that the disease may be mistaken for epithelioma, and there has been sufficient elaboration of that A second difficulty in histologic diagnosis arises only when the papillomatous cases of Darier's disease reach an extremely exaggerated form It is not until the papillae become most bizarre that the cells which cover them will approach the character of those that are seen in nevus syringocystadenomatosus

While I was sitting here I was wondering what was going through Dr McKenna's mind—whether, in his opinion, we Americans have been making a mountain out of a molehill, because Europeans know these conditions so well Dr Beerman indicated that this exaggerated form is known in Europe as well as over here, but that, as has been the case in America, not very much has been published I should like to hear from Dr McKenna on that point

It might occur to probably almost anybody that deficiencies in the diet are responsible At least, that theory would be the easiest way out, namely, that vitamin A deficiency would account for the difference in the incidence in Europe and in America We must remember, though, that concerning deficiency or other factors, even though attributing a condition to a certain thing would be easy or even logical, it need not necessarily be the true solution It must be remembered that when considering the role of geography one also has to consider the part played by the differences in race and racial characteristics For example, all of us present know the controversy as to whether yaws is an entity or whether it is syphilis modified by race Again, in pinta there is a disease of different appearance in Cuba and in Mexico The question is left open as to whether or not the factor of race is responsible for the clinical differences In hypertrophic Darier's disease, similarly, it need not necessarily be a vitamin deficiency, but the factor of race, that determines the clinical differences

DR ROBERT M B MCKENNA, London, England I should say that Darier's disease is not common in England, at the present time, at any rate The incidence does not seem to be increasing in any way

As for making comments on Dr Beerman's paper, I should like very much to discuss it, but I am afraid I am not prepared

DR HOWARD HAILEY, Atlanta, Ga I just want to make a correction The names of Hailey and Hailey have never been connected with Darier's disease but are associated with familial benign chronic pemphigus In the report on the condition under that title, as the senior author I stated and tried to emphasize that this condition is familial, benign and chronic The disease disappears, leaving no clinical evidence other than temporary pigmentation Recurrences follow at widely varying intervals, and, as the years go by, subsequent attacks become milder and are separated by longer intervals

DR HERMAN BEERMAN, Philadelphia I want to express my appreciation to the various discussers, especially Dr Weidman and Dr Ellis

With regard to the formation of lacunas, I am sorry, but I do not know how they form

There are variations of opinion as to the influence of vitamin A on Darier's disease Some people think that patients having Darier's disease are helped by the use of vitamin A The second patient mentioned herein received 250,000 units of vitamin A a day for a long time I put the statement that way because I do not know exactly how long, since he was in the medical service, records of which were not available, for part of the time

I want to apologize to the men from Boston for not having called Darier's disease White's disease, since the former is the more commonly used term, I have employed it

tests, determination of serum cholesterol and blood glucose, glucose tolerance tests, measurements of visual fields, roentgenography of the sella turcica and determinations of urinary gonadotropins and 17-ketosteroids

In the group of women with essential hirsutism there were 30 white female patients, 18 of whom were single and 12 married Twelve were obese and 18 of normal weight, 24 had a gynecoid habitus and 6 an android habitus and 23 had android pubic hair and 7 gynecoid pubic hair The clitoris was normal in all 30 patients, as were the breasts Seven of the patients had oily skin, with some acne, 6 had dry skin, and 16, normal skin Roentgenograms revealed a normal sella turcica for each of the 30 patients For the 22 patients who had visual field studies, these findings were normal Eleven patients had glucose tolerance tests, with low normal glucose tolerance curves observed in 4, and normal glucose tolerance curves in 7 The average age was 27 9, with a range from 15 to 43 The average menarcheal age was 13, with a range from 11 to 17 In 23 patients the menstrual flow was normal, in 5 the flow was short, and 2 had prolonged ovarian cycles The average weight was 147 pounds (67 Kg), with a range from 85 to 250 pounds (39 to 113 Kg) The weight at the time of examination averaged 154 2 pounds (70 Kg), with a range from 85 to 263 pounds (39 to 119 Kg) The average duration of the hirsutism was 6 43 years, with a range from one to fifteen years The average blood pressure was 124 systolic and 76 diastolic, with a range from 100 systolic and 60 diastolic to 155 systolic and 90 diastolic The basal metabolic rate averaged — 4 per cent, with a range from — 14 to 15 Urinary gonadotropins averaged 5 5 rat uterine units per twenty-four hours, with a range from 2 to 10 units, and 3 7 rat ovarian units, with a range from 2 to 8 units Urinary 17-ketosteroids averaged 10 6 mg per twenty-four hours, with a range from 5 4 to 20 3 mg

Ten patients with Cushing's syndrome, or adrenogenitalism, were studied All were white women, 7 of whom were married and 3 single The average age was 35, with a range from 26 to 43 The average menarcheal age was 13 years 9 months, with a range from 11 to 24 Two patients had had amenorrhea for one year, 1 for four years, and 1 for fourteen years The remaining patients had infrequent menstrual cycles, with usually scanty flow The average weight was 184 pounds (83 Kg), with a range from 100 to 300 pounds (45 to 136 Kg) The average weight at examination was 196 pounds (89 Kg), with a range from 137 to 325 pounds (62 to 147 Kg) The average duration of the hirsutism was eight years nine months, with a range from two to twelve years The average blood pressure was 156 systolic and 100 diastolic, with a range from 200 systolic and 100 diastolic to 116 systolic

demonstrated precocious hair growth In poorly fed, undernourished rats with adrenal hypertrophy, adrenalectomy resulted in increased growth of hair, which began within forty hours after the operation [5] Administration of estrogens retarded hair growth in rats, dogs and guinea pigs [6] This retardation of hair growth in rats could be prevented by the concomitant administration of androgens [6b] Plumage of birds, which is analogous to hair, was affected by gonadectomy [7] Removal of the thyroid and pituitary glands also influenced the growth of hair in various animals

One of the most obvious differences between hair growth in the animal and that in the human being is its development on contiguous body areas of man Danforth [2] stated that, although humoral control of human hair growth probably exists, the end product of each hair follicle is determined chiefly by constitutional factors within the hair cells It appears that some hair follicles are unaffected by the humoral differences of the male and the female, whereas others may be profoundly affected There apparently is a constitutional gradient which causes individual hair follicles to respond to hormonal influence Bissell and Williams [1] suggested that this constitutional characteristic may explain why two morphologically identical follicles may both give a fine body hair growth until puberty, when the product of one follicle may change to long terminal hair, although the product of the other follicle may not change throughout life

Danforth [2] offered the following classification of hair (1) general body hair (lanugo), which is uninfluenced by endocrine factors, (2) ambosexual hair of males and females, which is dependent on hormone stimulation and is apparently equivalent in the two sexes, pubic hair and axillary hair being examples of this type, and (3) truly sexual hair, which is represented by the beard of the male and, less clearly, by the terminal hair of the shoulders, of the anterior portion of the chest and of the abdomen The pattern of the hair of the head is probably a secondary sexual characteristic, as Bernstein and Robertson [8] showed that the weight per unit of hair length is greater in the male

5 Butcher, E O, and Richards, R A Relation of Adrenals to Retarded Hair Growth in Underfed Albino Rats, Endocrinology **25** 787 (Nov) 1939

6 (*a*) Gardner, W U, and Devita, J Inhibition of Hair Growth in Dogs Receiving Estrogens, Yale J Biol & Med **13** 213 (Dec) 1940 (*b*) Hooker, C W, and Pfeiffer, C A Effects of Sex Hormones upon Body Growth, Skin, Hair and Sebaceous Glands in Rat, Endocrinology **32** 69 (Jan) 1943

7 Allen, E, Danforth, C H, and Doisy, E A Sex and Internal Secretions, ed 2, Baltimore, Williams & Wilkins Company, 1939

8 Bernstein, M, and Robertson, S Racial and Sexual Differences in Hair Weight, Am J Phys Anthropol **10**.379 (July-Sept) 1927

COMMENT

These data emphasize commonly held impressions, namely, that the intensity, amount and distribution of hirsutism are not diagnostic evidence of endocrinopathy On the other hand, patients with established virilizing syndromes may have unimpressive hirsutism These facts emphasize that patients with hirsutism warrant capable medical consideration By no means, however, is it necessary that they undergo complicated special endocrinologic studies

If a woman with hirsutism has cyclic uterine bleeding of normal duration and has no symptoms or signs of virilization, it is unlikely that there is any endocrine cause for her hirsutism If it can be proved, by basal temperature graphs or by endometrial biopsy, that this patient has normal ovulatory function, it becomes practically certain that no endocrine disease exists, since normal ovarian function is not compatible with the virilizational syndromes

The symptom complex of gravest prognosis is amenorrhea and hirsutism By amenorrhea we mean an abscence of uterine bleeding for twelve months or longer

In conjunction with hirsutism, progressively less frequent and progressively scantier flow warrant definitive studies The basal temperature curves or endometrial biopsy data may confirm or negate the presence of qualitative failure in ovarian function, which may be related to endocrinopathic hirsutism

Other symptoms which have diagnostic and prognostic weight when conjoined with hirsutism include obesity, coarsening of the voice, psychosexual alterations and alterations in libido

The chief basis for the differentiation of essential hirsutism and hirsutism associated with endocrine disease lies in the clinical approach rather than in laboratory investigations A careful consideration of the patient's symptoms along the lines which have been discussed and a general physical examination, including a gynecologic study, should be ample for the screening of most patients Special studies which are of value, and which have been mentioned, include determinations of basal temperature curves and studies of endometrial biopsy specimens

Methods of hormonal quantitation which are adaptable to clinical practice yield a paucity of data in the differentiation of idiopathic hirsutism and endocrinopathic disease associated with hirsutism Commonly employed, but not infrequently misunderstood, are values for the urinary 17-ketosteroids A few statements about the significance of these substances seem justified In the female, the 17-ketosteroids represent normal degradational products of the metabolism of androgens and androgen-like substances of the adrenal cortex The urine of the normal female contains four of these adrenal 17-ketosteroids isoandrosterone,

Although Danforth stated that the general body hair, or lanugo, is not influenced by endocrine factors, it is difficult to explain the pronounced diminution of body hair in cases of panhypopituitarism and in cases of severe Addison's disease

Although hirsutism often characterizes virilizational syndromes, such as hypertrophy of the clitoris or deepening of the voice, it is seen frequently in women who are feminine, who menstruate normally and who bear children

In order for the factors influencing hair growth to be evaluated, the growth of hair in the male will be discussed Addison's disease may produce sparse pubic and axillary hair Prepuberal castration does not prevent the appearance of axillary and pubic hair Prepubescent males with panhypopituitarism acquire little, if any, axillary or pubic hair The adrenal cortex of man or woman, accordingly, can stimulate the development of ambosexual hair in the absence of the gonads

The truly sexual hair of the male, represented by the beard, is influenced by gonadal androgens This concept is supported by the absence of the beard in connection with prepuberal castration and its disappearance following postpuberal castration Hypopituitary males have no beard, whereas men with Addison's disease do not lose their beard Baldness is prevented by castration [13]

It may be concluded that there are three factors concerned with hair growth (1) a constitutional factor, representing the ability of an individual hair follicle to respond to endocrine stimuli, (2) a humoral factor, which supplies the stimulus for hair production to those follicles specifically sensitive to humoral action and, (3) local factors, such as blood supply, nerve supply and nutrition of the hair follicle

Hirsutism has been reported in cases of encephalitis, neuritis, mumps, gonadal teratoma, mental retardation and multiple sclerosis [14] Endocrinopathies commonly associated with hirsutism are basophilic tumors or hyperplasia of the pituitary gland (Cushing's syndrome), neoplasms or hyperplasia of the adrenal cortex (adrenogenitalism, or Cushing's syndrome), arrhenoblastoma and adrenal rest tumors of the ovary, tumors of the thymus, with secondary adrenal hyperplasia,[15] and luteomas [16]

13 Hamilton, J B Male Hormone Stimulation Is Prerequisite and Incitant in Common Baldness, J Invest Dermat **5** 473 (Dec) 1942

14 Schwartz, J H Hirsutism, Psychiatric Quart **16** 281 (April) 1942

15 Leyton, O, Turnbull, H M, and Bratton, A B Primary Cancer of Thymus with Pluriglandular Disturbance, J Path & Bact **34** 635 (Sept) 1931 Horrax, G Further Observations on Tumor of Pineal Body, Arch Neurol & Psychiat **35** 215 (Feb) 1936

16 Saphir, O So-Called Lutein Cell Tumors, Am J Obst & Gynec. **37** 1008 (June) 1939 Geist, S H, and Gaines, J A Diffuse Luteinization of Ovaries Associated with Masculinization Syndrome, ibid **43** 975 (June) 1942

Parenthetically, excess hair falls slowly, even when specific treatment of endocrinopathic hirsutism is observed In fact, except for coarsening of the voice and hypertrophy of the clitoris, hirsutism often constitutes the most persisting stigma of a virilizing syndrome after the virilizing tumor has been removed and there has been a return of normal ovarian function In view of these facts, it seems a rather ambitious hope to expect estrogen therapy to cause excessive hair to fall in essential hirsutism It seems to make little difference whether the estrogens are given orally or intramuscularly or are rubbed into the skin as ointments The empiric use of estrogens in treatment of patients with essential hirsutism and, by inference, with normal ovarian function not only may fail to relieve the hirsutism but also may bring about significant alterations in ovarian function The ovarian cycle, with both its qualitative and its quantitative values, may be disturbed and various irregularities of uterine bleeding precipitated Furthermore, local gynecologic disease, such as carcinoma or endometriosis, undiagnosed and unsuspected by those who practice empiricism, may be aggravated

The only therapeutic recommendations which can be given the patient with essential hirsutism are either that the patient forget and ignore the condition or that various palliative treatments, including shaving, manual epilation, bleaching and/or electrolysis, be tried

SUMMARY

The dermatologic and endocrinologic factors in normal and abnormal hair growth are discussed

The clinical and laboratory data concerning 30 patients with essential hirsutism and for 19 patients with endocrine disease associated with hirsutism are analyzed

Hirsutism warrants medical investigation Essential and endocrinopathic hirsutism may be differentiated by ordinary clinical investigations Special hormonal studies are of relatively little value in the differentiation

There is no specific endocrine treatment for essential hirsutism

828 Anderson Street

ABSTRACT OF DISCUSSION

DR HERBERT RATTNER, Chicago Hirsutism, despite its common occurrence, remains one of the obscure and unsolved problems of medicine As Dr Callaway and his associates indicated, it is a problem that sometimes assumes proportions of great importance It may be noted that among their patients there were some with psychoneuroses severe enough to cause them to contemplate suicide. Hirsutism is an abnormal condition difficult to explain because even the control of normal hair growth is obscure and unexplained Hair growth is a complex mechanism influenced, apparently, by constitutional, endocrinologic, genetic and racial factors, and perhaps by local factors, such as follicular nutrition, blood

17-Ketosteroids—The method used for the determination of urinary 17-ketosteroids is an adaptation by one of us (A A S) of various standard procedures [20] Fractional (one-eighth to one-fourth) twenty-four hour specimens of urine of three to four successive days are used The method begins with acid hydrolysis of the urine under reflux, followed by extraction with carbon tetrachloride, employing a continuous extractor The carbon tetrachloride is removed by vacuum distillation, leaving the urinary extract, a crude residue The residue is passed through several purifications, including a procedure with the Girard reagent T For final assay, the Zimmermann meta-dinitrobenzene color reaction is employed, according to Holtorff and Koch [20e] A Klett-Summerson photoelectric colorimeter is used to measure color intensity Pure crystalline androsterone is the standard The range of values for normally menstruating adult women is 4 0 to 14 0 mg per twenty-four hours

The assay of urinary steroids was discussed in a recent symposium by a number of English workers, including Bishop [21] and Callow [22] Friedgood and Whidden,[23] among others, also considered the assay of crystalline urinary androgens

CLINICAL DATA

The data on 30 patients with idiopathic hirsutism are contrasted with those for patients with known endocrinologic disorders, including 10 with Cushing's syndrome, or adrenogenitalism, and 9 with virilizing tumors of the ovary

The entire group was analyzed with reference to age, color, sex, marital status, whether or not pregnancy had occurred, age at menarche, ovarian cycle, libido, previous endocrine therapy, average weight and present weight and the duration of the hirsutism Physical examination included an evaluation of the blood pressure, habitus, skin, hair distribution, degree of hirsutism, degree of obesity, thyroid function, bone age, breasts and genital organs Laboratory studies included basal metabolic

20 (*a*) Callow, N H, Callow, R V, and Emmens, C W Colorimetric Determination of Substances Containing Grouping—CH_2CO—in Urine Extracts as Indication of Androgen Content, Biochem J **32** 1312 (Aug) 1938 (*b*) Talbot, N B, Butler, A M, and MacLachlan, E The Colorimetric Assay of Total, α-, and β-17-Ketosteroids in Extracts of Human Urine, J Biol Chem **132** 595 (Feb) 1940 (*c*) Cohen, R I, and Salter, W T Urinary 17-Ketosteroids in Metabolism Standardized Chemical Estimation, ibid **152** 489 (March) 1944 (*d*) Hershberg, E B, and Wolfe, J K A Rapid Extractor for Urinary Steroids, ibid **133** 667 (May) 1940 (*e*) Holtorff, A F, and Koch, F C Colorimetric Estimation of 17-Ketosteroids and Their Application to Urine Extracts, ibid **135** 377 (Sept.) 1940

21 Bishop, P M F The Clinical Significance of Urinary Steroid Assays, J Endocrinol **5** 81 (Jan) 1948

22 Callow, R K The Chemical Estimation of Urinary Neutral 17-Ketosteroids, J Endocrinol **5** 67 (Jan) 1948

23 Friedgood, H B, and Whidden, H L Assay of Crystalline and Urinary Androgens, with Special Reference to Their Measurement by Colorimetric Method, New England J Med **220**.736 (May 4) 1939

DR GROSVENOR W BISSELL, Chicago In the cases of idiopathic hirsutism my associates and I have studied, clinical observations and chemical and endocrinologic studies have been similar to those reported In our experience, overweight seems to have been more commonly observed, however, and it has been our observation that this increase in body weight frequently followed the appearance of the abnormal facial hair Since the relation of obesity to psychogenic disturbances is now well recognized, we have wondered whether the increase in weight is not a reflection of the patient's psychiatric reaction to the appearance of the hirsutism rather than the result of any more specific metabolic cause We have likewise found a lessened carbohydrate tolerance in a large percentage of our patients, but this, again, may be predicated on the greater occurrence of obesity in our group, since many obese persons have abnormal glucose tolerance curves which revert to normal if normal weight is resumed

I should like to reemphasize Dr Callaway's appeal for a pertinent clinical approach to the subject of hirsutism The absence of accompanying signs of virilism is an important clinical confirmation that one is dealing with the idiopathic variety of hirsutism Dr Callaway's use of determinations of basal body temperatures and of biopsies of endometrial tissue to establish the presence of ovulatory cycles seems to us to be a particularly valuable adjunct in the recognition of idiopathic hirsutism, especially in cases in which there are accompanying menstrual irregularities

The racial and familial genetic history of the patient must likewise be carefully appraised

I should like to mention the occurrence of a transient, self-limited type of idiopathic hirsutism which is occasionally observed This type of hirsutism is sometimes seen during the course of pregnancy and may persist until after delivery or disappear even before delivery has taken place A family history of the occurrence may sometimes be elicited My associates and I have likewise seen transient hirsutism follow severe thermal burns It has been reported also sometimes to accompany states of extreme starvation

We are in complete agreement with Dr Callaway with regard to the treatment of idiopathic hirsutism No specific therapy is presently available, and, although local therapy of the condition is not particularly successful, this form of treatment, together with psychotherapy and reassurance, is the only one that we feel is justified at present

It is obvious from what has been presented that this condition of unknown etiology needs much more intensive investigation The frequent occurrence of the abnormality among certain families and racial groups would seem to indicate that part of the problem must await solution by the geneticist

Although a specific endocrine cause of this disorder is not presently demonstrable, there are certain leads which suggest that the development of better technics may result in the demonstration of a causal endocrine relation Dr Callaway has mentioned the desirability of determining androgen-estrogen ratios for these patients Glass and Bergman have performed such a study on a small group of idiopathically hirsute women and have demonstrated that the ratio of androgens to estrogens was greater in these subjects than in normal women

Idiopathic hirsutism frequently makes its appearance at the time of the menarche, pregnancy or the menopause It may transiently accompany severe thermal burns or pronounced states of inanition All these events are associated with altered function of the adrenal cortex It would seem, then, that although present assay methods do not demonstrate clearly such a connection, this disorder may have at least a component of adrenal malfunction There is also recent evidence

and 78 diastolic The habitus of all was android The hair distribution was android in 9 patients and gynecoid in 1 patient Nine of the 10 persons were obese, 9 had normal breasts, and 1 had small breasts The clitoris was normal in all The skin in 8 was normal, and in 2 it was oily, with an acneform eruption The basal metabolic rates averaged − 4 per cent, with a range from 17 to + 26 per cent Serum cholesterol values averaged 200 mg per hundred cubic centimeters, with a range from 160 to 270 mg Blood glucose values averaged 138 5 mg. per hundred cubic centimeters, with a range from 80 to 218 mg Glucose tolerance tests yielded diabetic curves for 5 patients and normal curves for 5 patients Visual fields and roentgenograms of the sella turcica were normal in all patients The output of urinary gonadotropins averaged 8 rat uterine units per twenty-four hours, with a range from 2 to 14 units, and 3 75 rat ovarian units per twenty-four hours, with a range from 2 to 6 units Urinary 17-ketosteroids averaged 13 25 mg per twenty-four hours, with a range from 6 to 26 3 mg

All the 9 patients with masculinizing tumors of the ovaries were white The average age was 29 4, with a range from 22 to 41 The average menarcheal age was 12, with a range from 11 to 14 One patient had had amenorrhea for fifteen months, 1 for eighteen months, 1 for twenty-four months and 1 for thirty-six months The rest of the patients had infrequent cycles and usually scanty flow The average weight was 141 pounds (64 Kg), with a range from 120 to 180 pounds (54 to 81 Kg) The average weight at examination was 148 pounds (67 Kg), with a range from 120 to 199 pounds (54 to 90 Kg) The hirsutism had been present for an average duration of five years nine months, with a range from two to twelve years The blood pressure averaged 125 systolic and 84 diastolic, with a range from 140 systolic and 100 diastolic to 116 systolic and 60 diastolic Five were of android habitus, and 4, of gynecoid habitus The hair distribution in all was android Four of the 9 were obese, all 9 had normal breasts, 5 had a large clitoris, and 4 had a normal clitoris Five had oily, acneform skin, and 4, normal skin The basal metabolic rate averaged 3 per cent, with a range from 26 to + 19 per cent The serum cholesterol averaged 195 mg per hundred cubic centimeters, with a range from 170 to 230 mg The blood glucose averaged 98 mg per hundred cubic centimeters, with a range from 84 to 108 Glucose tolerance tests for 8 of the patients gave normal curves The visual fields and roentgenograms of the sella turcica were normal in all 9 Urinary gonadotropins averaged 7 5 rat uterine units per twenty-four hours, with a range from 2 to 24 units, and 5 rat ovarian units per twenty-four hours, with a range from 2 to 16 units Urinary 17-ketosteroids averaged 18 7 mg , with a range from 3 1 to 49 7 mg

DR. J LAMAR CALLAWAY, Durham, N C I should like to say again, as I did in the paper, that many of our studies were patterned after those of Drs Bissell and Williams Our findings were somewhat similar to theirs

Dr Bissell called attention to the transient hirsutism that sometimes occurs at the menarche, during pregnancy and at the menopause This needs no specific treatment

Dr Rattner was correct in indicating that all patients with hirsutism should have a complete clinical and laboratory evaluation I should like to emphasize that laboratory findings should be evaluated very critically, however

Dr Lamb pointed out, as did Dr Bissell, that newer and more accurate clinical and laboratory methods for evaluating ketosteroid determinations are now beginning to be developed Perhaps physicians will be in a position soon to make androgen determinations

I was much interested in Dr Oppenheim's report of pubic and genital hair growth as a result of local irritation from the preparations which he used. This observation may possibly have some significance in connection with facial hirsutism

dehydroisoandrosterone, androsterone and etiocholane-3α-ol-17-one. Although these four products are derivatives of androgens, they vary in their true androgenism The most active is androsterone, the next most active, dehydroisoandrosterone, and the next after that, isoandrosterone Etiocholane-3α-ol-17-one is biologically inactive

Urinary 17-ketosteroids are reported in terms of milligrams excreted per twenty-four hours The milligram unit has no biologic equation, it is determined colorimetrically It is possible for the androgenicity of samples of urine yielding the same values for 17-ketosteroids to vary 1,000 per cent or more

The determination of alpha and beta urinary 17-ketosteroids, a procedure which is not particularly difficult, does not aid materially in verifying the presence or absence of increases in 17-ketosteroids of high androgenicity or of low androgenicity

Urinary 17-ketosteroids and urinary androgens, therefore, cannot be considered the same If it were possible to quantitate urinary androgens as a clinical procedure and simultaneously to compare these results with those for urinary estrogens, the androgen-estrogen ratio of a patient could be established Such a ratio would express the degree of androgenicity and the degree of estrogenicity of the patient These data might well prove helpful in the evaluation and study of patients with idiopathic hirsutism Such determinations are not practical with present methods of hormone study

The determination of the androgen-estrogen ratio is not necessary to establish a diagnosis of endocrinopathic hirsutism Ordinary, careful clinical investigations can do this These data, however, may elucidate the problem of essential hirsutism They may confirm or negate various theories which have been propounded as to the etiology of the condition, including those of relative or borderline hyperplasia of the adrenal cortex and of incomplete differentiation of the female gonad, with a preponderance of medullary structures remaining unsuppressed

The 30 women with essential hirsutism who have been studied gave no evidence of ovarian failure, in direct contrast to the patients presented with proved endocrinopathies Some of these women to be specific, one third had prolonged ovarian cycles, with a maximum duration of sixty days, but all had flows of normal amount and duration These not uncommon variations in cycle length were not associated with any evidence of endocrine disease Furthermore, they were not associated with any significant alterations in urinary 17-ketosteroids For the 5 patients who had 17-ketosteroid values above the upper range of what is considered normal, the average cycle length was forty-four days, with a range from twenty-eight to sixty days

Whatever the cause of essential hirsutism is, by definition, it is not known Accordingly, there is no specific treatment for the condition

has a profound beneficial effect on the abnormalities of the spinal fluid and the clinical course of neurosyphilis All these papers are clinical, and, except for the reports of Rose [4] and Curtis,[7] the use of penicillin alone as the therapeutic agent is stressed The latter authors discuss the therapeutic effects of penicillin alone as well as of penicillin combined with fever therapy

A recent publication on this subject is that of Stokes and associates [2d] These authors reported the effects of the use of penicillin alone in treatment of 361 patients with neurosyphilis who were observed for 90 to 1,100 days Their findings indicate that in its effects treatment with penicillin alone is at least equal to a combination of fever therapy and chemotherapy and is superior in dealing with some forms of neurosyphilis The authors stated the conclusion that penicillin seems to be more effective in controlling the mechanism which produces abnormalities in the spinal fluid than in controlling that which causes the symptoms of neurosyphilis On the other hand, malarial or fever therapy affects the symptom-producing mechanism more than it does that which leads to spinal fluid abnormalities These authors expressed the opinion, as have others, that a combination of fever therapy and treatment with penicillin may give a prompter result than does either alone

COMBINATION OF PENICILLIN WITH FEVER THERAPY

Previous to the introduction of penicillin, fever therapy had been established as the procedure of choice for the treatment of various forms of symptomatic neurosyphilis and resistant asymptomatic neurosyphilis

Eagle [9] recently showed that in vitro the spirocheticidal property of penicillin is enhanced by elevation of the temperature of the testing solution In a solution of penicillin containing 25 to 250 units per cubic centimeter he found that the following conditions exist

At 8 C all the T pallidum remain viable for twenty-four hours

5 Callaway, J L, and others The Use of Penicillin in the Treatment of Syphilis of the Central Nervous System Report of One Hundred Patients, Am J Syph, Gonor & Ven Dis **30** 110-124 (March) 1946

6 Koteen, H , Doty, E J , Webster, B, and McDermott, W Penicillin Therapy in Neurosyphilis, Am J Syph, Gonor & Ven Dis **31** 1-13 (Jan) 1947

7 Curtis, A C Neurosyphilis Treatment with Penicillin Alone and with a Combination of Penicillin and Malaria, read before the Thirteenth Venereal Disease Control Seminar, United States Public Health Service, San Francisco, Calif, May 26, 1947

8 O'Leary, P A , Brunsting, L A , and Ockuly, O Penicillin in the Treatment of Neurosyphilis, J A M A **130** 698-700 (March 16) 1946

9 Eagle, H , Magnuson, H J , and Fleischman, R The Effect of Hyperpyrexia on the Therapeutic Efficacy of Penicillin in Experimental Syphilis, Am J Syph, Gonor & Ven Dis **31** 239-245 (May) 1947

supply and nerve supply Of these, the endocrinologic factor has long been considered one of the more important influences The literature contains ample experimental and clinical evidence to suggest a strong link between the function of the various endocrine glands and hirsutism Unfortunately, the experimental evidence is not always applicable to man, whose hairy system is unique and complicated, and while hirsutism has been reported in many pathologic entities involving endocrine glands, on occasion women with virilizing syndromes may have but little hirsutism, while others with abundant hair growth may exhibit no evidence of endocrine abnormalities In an attempt to solve this particular puzzle, Dr Callaway and his co-workers have studied two groups of patients with the hope of finding a common denominator that would serve as a clue to the mystery of hirsutism Unfortunately, no such factor was found Studies were conducted both clinically and in the laboratory, with special emphasis on endocrine factors Of all the technics employed, it was found that the clinical investigations proved to be most significant, that clinical investigations alone were sufficient to differentiate idiopathic hirsutism from the endocrinopathic variety and that special hormonal studies were of little value It is stated specifically that the chief reliance for the differentiation of the two varieties of hirsutism lies in the clinical approach rather than in laboratory investigations and that it is unnecessary to institute complicated special endocrinologic studies I should like to amend this view somewhat by repeating the advice offered us at Michael Reese Hospital by Dr Rachmael Levine, the endocrinologist He advocated what he called a whole approach, without the limiting of investigations to necessary technics only In all medical problems that are not fully understood it is desirable to attack from all sides, to undertake complete clinical and laboratory studies in a large number of cases, if possible, even though it may be anticipated that these studies may furnish no information of value Indeed, dermatologists might well heed the example of the oncologists, who are studying their problem from all angles with the hope that one of their studies may lead to a solution Laboratory and clinical methods complement each other Accordingly, in the investigation of a case of permanent hirsutism, the minimum procedures for endocrinologic studies should consist of determinations of basal body temperature, study of vaginal smears in the first half of the menstrual cycle and a pregnandiol test in the second half to determine the status of estrogen and corpus luteum, respectively, and the measurement of urinary 17-ketosteroids These highly desirable and pertinent procedures are neither expensive to the patient nor too complicated to be carried out in a well conducted laboratory Only by means of such routine studies in a large number of cases might one conceivably uncover a steroid abnormality or some other change of significance

The authors' conclusions are correct Clinical investigations are of greatest importance, hormonal studies most often offer little of value in solution of the problem of idiopathic hirsutism, there is no specific endocrinologic treatment for the condition, and empiric treatment with endocrinal substances is to be decried

Nevertheless, the subject is of such importance and the problem so complex that similar studies should be encouraged and carried further Knowledge of the endocrine glands is developing constantly Perhaps newer knowledge of steroid chemistry will disclose the cause of hirsutism I hope that Dr Callaway and his associates will continue with their study and that they will continue to complement their clinical studies with laboratory investigations The subject is an important one, if only because the condition causes distress to such large numbers of women This paper by Dr Callaway and his co-workers should stimulate dermatologists to further study

with fever therapy O'Leary,[8] in a small number of cases of neurosyphilis, noted no increased effect when the administration of penicillin was combined with fever therapy

PLAN OF STUDY

In this paper we wish to report on our experience with the combined use of penicillin and artificial fever in the treatment of neurosyphilis This work began in March 1945 and was continuing at the time of writing Until July 1946 penicillin sodium in aqueous solution, 40,000 units every three hours, administered intramuscularly, was given for fourteen to fifteen days The treatment was begun with a dosage of 10,000 units every three hours for twelve hours, and then 20,000 units every three hours for twenty-four hours, after which time it was continued for fifteen days at the full dosage of 40,000 units A total dosage of 4,000 000 to 4,500,000 units was administered While the patient was hospitalized he was given fever therapy, consisting of the induction of temperatures of 40 to 40 5 C (104 to 105 F) for five hours, twice weekly The fever was induced by means of the blanket method, a simple mechanical means described by one of us (N N E) in 1937 [13] Each patient received, as a rule, four fever treatments during his two weeks of hospitalization These were followed by a weekly fever treatment until a total of ten to fifty hours of fever had been given

Since July 1946 a majority of the patients have been given 300,000 units of penicillin calcium suspended in peanut oil containing 4 5 per cent white wax U S P (the Romansky formula) intramuscularly, once daily for twenty days, or a total of 6,000,000 units Fever therapy as previously described was administered weekly during and subsequent to the penicillin therapy until ten fever treatments had been given This ambulatory method of penicillin therapy facilitated the work as it lessened the expense and eliminated the two week hospitalization period The patient was hospitalized for twenty-four hours during each fever treatment

Follow-up observations consisted of repeated clinical and laboratory examinations at intervals of from four to six months Additional treatment was given whenever the clinical or serologic response did not appear satisfactory

CLINICAL MATERIAL

A total of 87 patients with various forms of neurosyphilis were treated with penicillin as well as artificial fever Of this group 55 patients have been followed for one hundred and twenty days or longer, and sufficient data as to their clinical and serologic progress are available

13 Epstein, N N The Blanket Method of Inducing Artificial Fever, Arch Phys Therapy **18** 199-205 (April) 1937

by Albright that the adrenal response to stress in idiopathically hirsute women is greater than in the normal woman and more closely resembles that of the normal man

Dr Callaway has pointed out the disparity between the 17-ketosteroid assay and fractionated androgen assays on the same subject I should like further to point out that these are both tests of the end results of any given person's steroid metabolism, an accurate estimation of their individual significance or their relation to each other must await clarification of the intermediary metabolism involved, about which virtually no data exist

Obviously, a final answer to this problem will come only when there has been more intensive study of the disorder I congratulate Dr Callaway and his associates on their paper, which represents a valuable and needed contribution to the clarification of this difficult condition

Dr John H Lamb, Oklahoma City At the annual meeting of the Association for the Study of Internal Secretions, on June 18, 1948, Dr Roney presented an interesting and stimulating paper on pseudoglandular disturbance which may throw light on the problem of essential hirsutism He stated that, in general, hormonal effects depend on end organ sensitiveness, as well as on the active hormone, and that normal levels of the stimulating hormone may invoke a greater intensity of response because of this increased end organ sensitivity He included essential hirsutism in this category I wish to point out that about forty-two other steroids have now been isolated from normal and pathologic urine It is a possibility that future investigations may relate one of these new steroids to specific conditions, such as the stimulation of excessive hair growth in women

Dr. Maurice Oppenheim, Chicago About thirty years ago, in the department of dermatology in the Wilhelminen Hospital, Vienna, injections of argyrol,® (a preparation of silver with a protein produced by the electrolysis of serum albumin), strong protein silver N F (protargol®) and silver nitrate in various concentrations were given to infants and babies infected with gonorrhea, and the treatment was continued for a long time two months, three months and six months Then my associates and I made the normal irritation and stimulation tests to find out whether the babies and infants were free from gonococci At that time there was no treatment with estrogen or with penicillin, but only the local treatments were possible

In the course of this treatment, we saw, in some of these subjects, hair growing on the labia majora, on the anus and on the pubes There were no lanugo hairs, but bristle and long hairs, not many

We concluded that as a consequence of this treatment the hair growth was produced We had no explanation for this

Later we found that most of those children who showed the hair growth started to masturbate So sexual development was stimulated by this treatment We used only local treatment at the time No external irritation was visible, the other children did not show this hair growth There were no black-stained pre-existing hairs which had been overlooked We came to the conclusion that the repeated local treatment of the genital area was in some way stimulating the ovarian function to produce more hormones, so that the hair growth was initiated This is only a small experimental contribution to this question I am sorry that I cannot present the slides which I made many years ago But it is evident that by local irritation of the genitals, vulva, urethra and vagina one can produce, in some persons, an abnormal hair growth on the pubic and genital area

In the few patients with meningovascular syphilis, changes in objective and subjective symptoms were readily observed In 1 patient, diplopia due to a right-sided oculomotor paralysis cleared within ten days after treatment was instituted, another patient with excruciatingly severe pains in the head obtained complete relief in five days, the third patient, who had meningovascular neurosyphilitic paresis of the left lower limb and motor aphasia, responded within a few months

It was our impression that the patients with objective and subjective symptoms of neurosyphilis responded more promptly to penicillin and fever therapy than patients treated in the past had responded to chemotherapy combined with artificial fever therapy

In most instances the clinical response paralleled the changes in the spinal fluid Changes in spinal fluid probably reflect the effect of the treatment more accurately than can clinical observation

TABLE 2—*Changes in Patterns of the Spinal Fluid*

Grade	Before Treatment	120 to 365 Days After Treatment	365 Days + After Treatment
1	6 (11 1%)	20 (37 0%)	8 (34 4%)
2	17 (31 5%)	24 (44 4%)	2 (8 6%)
3	31 (57 4%)	5 (9 3%)	4 (17 2%)
Normal	0	5 (9 3%)	9 (38 7%)
Total	54	54	23

CHANGES IN THE SPINAL FLUID

The spinal fluid abnormalities will be considered from two standpoints, namely (1) the general pattern of the spinal fluid and (2) the individual constituents and reactions of the spinal fluids, i e, the cell count, the protein content, the colloidal gold reaction and the Wassermann reaction Moore's [14] classification of spinal fluid pattern or formulas was used to designate the degree of abnormality present Grade 1 refers to minimal changes, grade 2 to changes slightly more abnormal than those of grade 1, and grade 3, to a distinctly abnormal fluid, i e, one with the "paretic" formula

PATTERNS OF THE SPINAL FLUID

Table 2 shows the distribution of spinal fluid patterns before and after treatment It can be seen that the percentage of patients with grade 3 spinal fluids is appreciably decreased by treatment, i e, from 57 4 per cent to 9 3 per cent within one year after treatment Simul-

14 Moore, J E , Kemp, J E., and others The Modern Treatment of Syphilis, ed 2, Springfield, Ill, Charles C Thomas, Publisher, 1941

TREATMENT OF NEUROSYPHILIS WITH PENICILLIN COMBINED WITH ARTIFICIAL FEVER

NORMAN N EPSTEIN, M D
AND
JULES M KEY, M D
SAN FRANCISCO

THE VALUE of penicillin as a therapeutic agent in neurosyphilis is well established The exact degree to which it may be relied on to prevent the development of neurosyphilis or to repair pathologic processes produced by Treponema pallidum in the central nervous system has not been determined Since the introduction of penicillin as an antisyphilitic remedy by Mahoney [1] in 1943, much research work has been done in the field of neurosyphilis The early optimism expressed by these workers appears to be justified

The papers of Stokes,[2] Moore,[3] Rose,[4] Callaway,[5] Koteen,[6] Curtis,[7] O'Leary [8] and their associates amply confirm the fact that penicillin

Read at the Sixty-Eighth Annual Meeting of the American Dermatological Association, Inc, San Diego, Calif, April 27, 1948

From the Department of Dermatology of the Division of Medicine of the University of California Medical School and the Department of Dermatology of the Mount Zion Hospital

1 Mahoney, J F , Arnold, R C, and Harris, A D Penicillin Treatment of Early Syphilis, Ven Dis Inform **24** 355-357 (Dec) 1943

2 (*a*) Stokes, J H, and others The Action of Penicillin in Late Syphilis, Including Neurosyphilis, Benign Late Syphilis and Late Congenital Syphilis Preliminary Report, J A M A **126** 73-79 (Sept 9) 1944 (*b*) Gammon, G D, and others Penicillin in Neurosyphilis Effect on Blood and Spinal Fluid, ibid **128** 653-654 (June 3) 1945 (*c*) Stokes, J H , Boerner, F , Hitchens, A P, and Nemser, S Penicillin Alone in Neurosyphilis, ibid **131** 1-7 (May 4) 1946 (*d*) Stokes, J H , Steiger, H P, and Gammon, G D Three Years of Penicillin Alone in Neurosyphilis, Am J Syph, Gonor & Ven Dis **32** 28-42 (Jan) 1948

3 Reynolds, F W , Mohr, C F, and Moore, J E Penicillin in the Treatment of Neurosyphilis II Dementia Paralytica, J A M A **131** 1255-1260 (Aug 17) 1946 Moore, J E, and Mohr, C F Penicillin in the Treatment of Neurosyphilis Asymptomatic Neurosyphilis, Am J Syph, Gonor & Ven Dis **30** 405-419 (Sept) 1946

4 Rose, A S, and others The Penicillin Treatment of Neurosyphilis Preliminary Report of Seventy Cases Followed from Four to Twelve Months, Am J Syph, Gonor & Ven Dis **29** 487-493 (Sept) 1945 Rose, A S, and Solomon, H C Penicillin in Treatment of Neurosyphilis Study of One Hundred Cases Followed Twelve Months or More, J A M A **133** 5-10 (Jan 4) 1947

(Footnotes continued on next page)

CHANGES IN CELL COUNT

The cell count in the spinal fluid was distinctly influenced by the administration of penicillin combined with artificial fever therapy In a large majority of instances the cell count returned to normal during the first year of observation This change was usually noted after the first follow-up examination, i e, one hundred and twenty days after the treatment had been given The abnormal cell counts varied from 8 to 265 cells per cubic millimeter Patients with high cell counts responded as promptly as did those with lower counts

TABLE 5—*Changes in Cell Count*

Abnormal Before Treatment	Period of Observation	Decreased to Normal	Decreased	Increased	No Change
32	120 to 365 days	28 (87 6%)	2 (6 2%)	2 (6 2%)	0
13	365 days +	11 (84 6%)	2 (15 4%)	0	0

TABLE 6—*Changes in Colloidal Gold Curve*

Grade of Abnormality	No of Cases Before Treatment	No of Cases 120 to 365 Days After Treatment	No of Cases 365 + Days After Treatment
1 (slight)	5	9 (20 8%)	2 (13 2%)
2 (moderate)	10	12 (27 6%)	1 (6 6%)
3 (appreciable)	28	4 (9 2%)	3 (19 8%)
Normal	0	18 (42 4%)	9 (60 4%)

TABLE 7—*Change in Grade 3 Colloidal Gold Curves*

No of Patients with Grade 3 Curves Before Treatment		No Reversed to Normal	No Reversed to Near Normal	Total Improved
28	First year of observation	11 (38 5%)	5 (17 5%)	16 (56 0%)
13	Second year of observation	9 (69 0%)	1 (7 7%)	10 (76 7%)

CHANGES IN PROTEIN CONTENT

The protein content of the spinal fluid was also greatly influenced by the treatment Inasmuch as quantitative determinations were not done routinely, accurate figures cannot be given The response, however, seemed to parallel the changes in the cell count, although it was not achieved as promptly

CHANGES IN THE COLLOIDAL GOLD REACTION

The colloidal gold reaction showed a remarkable change toward normal, more so with this treatment than with any other method which

At 22 to 23 C 10 per cent of the T pallidum remain viable for twenty-four hours

At 32 to 33 C 1 per cent of the organisms remain viable for twenty-four hours

At 39 to 40 C only 0 02 per cent of the organisms remain viable for twenty-four hours

It should be pointed out that temperatures of 39 and 40 C are lethal to T pallidum This does not vitiate the fact that Eagle's experiments show a definite increase in the spirocheticidal effect of penicillin in vitro under conditions of increased temperature of the testing solutions

Eagle further showed that the curative dose of penicillin in rabbit syphilis is reduced eight to ten times by the elevation of the animal's temperature 3 to 4 F over a ten-hour period during the administration of the penicillin This work indicates that the favorable effect of fever on penicillin therapy is accomplished probably by (1) its enhancing the therapeutic efficacy of the penicillin and (2) a synergistic or additive effect

Eagle,[10] as well as Boak,[11] Carpenter[12] and their co-workers, showed that T pallidum becomes more vulnerable to water-soluble bismuth compounds, neoarsphenamine and oxophenarsine hydrochloride (mapharsen®) when exposed to these drugs under conditions of increased temperature

When one considers the aforementioned experimental findings and the definite beneficial effects of artificial fever on the clinical course of neurosyphilis, it appears logical that a combination of penicillin and fever therapy should produce better effects than either procedure alone Moore[8] recommended the combined use of penicillin and fever for certain forms of neurosyphilis Rose[4] stated the opinion that the administration of penicillin alone has not proved as effective as has treatment with penicillin and fever Curtis[7] expressed the belief that the administration of penicillin was somewhat more effective when combined with fever therapy than when used alone Later, at the meeting of the American Academy of Dermatology and Syphilology in December 1947, he stated the conclusion that penicillin was as effective in the treatment of neurosyphilis when used alone as when combined

10 Eagle, H The Minimal Effective Concentrations of Arsenic and Bismuth Compounds on T Pallidum in Vitro in Relation to the Therapeutic Dose, Am J Syph, Gonor & Ven Dis **23** 310-318 (May) 1939

11 Boak, R A, Carpenter, C M, and Warren, S L The Concurrent Treatment with Fever and Neoarsphenamine of Experimental Syphilis in Rabbits, Am J Syph, Gonor & Ven Dis **26**·282-290 (May) 1942

12 Carpenter, C M, Boak, R. A, and Dorn, F S The Concurrent Treatment of Experimental Syphilis with Fever and Mapharsen, Am J Syph, Gonor & Ven Dis **31** 498-505 (Sept) 1947

had his first fever treatment twelve hours before He then became disoriented, confused, incontinent, agitated and convulsive He was transferred to the detention ward of the San Francisco Psychopathic Hospital, where he recovered uneventfully

A second patient, not included in this series, had a similar reaction He was a white man, aged 38, who had been receiving 50,000 units of aqueous penicillin sodium intramuscularly every three hours around the clock for five days, subsequent to an emergency appendectomy Reexamination showed the presence of dementia paralytica clinically and serologically On the fifth postoperative day, the patient became violently agitated, disoriented and confused and had visual hallucinations Penicillin therapy was discontinued, and the reaction subsided within forty-eight hours Penicillin therapy was reinstituted without further untoward effects

Further evidence of therapeutic shock was noted in the group of 28 patients who received aqueous penicillin sodium at regular intervals around the clock In 14 of these the temperature rose, varying between 37 4 and 39 4 C (99 3 and 102 9 F) within twenty-four hours of the institution of penicillin therapy In the majority of the patients who exhibited this early febrile response, the temperature did not rise above 38 C (100 4 F) and it receded to normal within twelve hours

Urticaria was noted in 3 of the 87 patients treated, 2 of the patients had received aqueous penicillin sodium, and 1 patient had been given penicillin in oil and wax A dermatophytosis-like reaction of the hands and feet occurred in 1 patient, and an erythematous eruption of the groins, lower portion of the abdomen and thighs was observed in another The latter case was the only one in which penicillin therapy had to be discontinued

Local reactions to penicillin in oil and wax were common during the first year of its use However, after the introduction of the emulsions which are fluid at room temperature, no severe local reactions at the site of the injections were noted

The fever therapy was well tolerated in most instances and in only 1 case in this series was it necessary to discontinue the fever therapy because of respiratory difficulty Nausea and vomiting, immediately after treatment, occurred in several patients In 1 case the fever therapy was discontinued after nine treatments because of these symptoms Herpes simplex was common after the first treatment

COMMENT

There is no doubt that penicillin is the most effective therapeutic agent for neurosyphilis which has been introduced up to the present time Stokes [2d] found that the best therapeutic response that one can expect to obtain from penicillin alone, regardless of dosage or repeti-

for presentation in this report The entire group of 87 patients, however, will be discussed from the standpoint of reactions to treatment

Twenty-eight patients received penicillin sodium in aqueous solution, together with fever therapy, 20 received penicillin in oil and wax, and 7 received at least one course of each type of penicillin, together with fever therapy Table 1 shows the clinical diagnoses for the entire group of 55 patients

CLINICAL RESPONSE

The number of patients in each of the diagnostic categories was too small for statistical analysis of the clinical effects which were produced by the treatment The group with dementia paralytica was the largest, and some conclusions can be drawn concerning the efficacy of the combination of penicillin and fever therapy in these patients No striking effects were noted in the group with tabes dorsalis

Of the 25 patients with dementia paralytica, 8 showed pronounced clinical improvement, 10, moderate improvement, 2, slight improvement, and 5, no change The patients with early dementia paralytica responded best, 1 patient with acute symptoms had remarkable clearing, and 2 with advanced, appreciable deterioration did well clinically, considering the degree of mental deterioration which was present prior to the institution of treatment

TABLE 1—*Patients with Neurosyphilis Treated with Penicillin and Artificial Fever*

	Asymptomatic Neurosyphilis	Dementia Paralytica and Its Tabetic Form	Tabes Dorsalis	Diffuse Neurosyphilis	Meningovascular Neurosyphilis	Hereditary Neurosyphilis
Number of patients	16	25	4	3	3	4

In the 4 patients with optic atrophy, the vision remained stationary in 3 and was slightly decreased in 1

The clinical response of patients with neurosyphilis to a given method of treatment is very difficult to evaluate, particularly in cases of persons with dementia paralytica Often the subjective symptoms are vague, and changes in these symptoms may be influenced by suggestion A large majority of these patients experienced a definite improvement in general well-being In the group with dementia paralytica, a decrease in nervousness, indecisiveness and uncertainty was noted Whenever there were clearcut symptoms, such as decided emotional instability, confusion and loss of memory, the treatment frequently gave noticeable relief The pains of tabes were not noticeably benefited

infrequent in neurosyphilitic patients receiving penicillin In our series of 87 patients with neurosyphilis there was only 1 patient in whom definite neurologic symptoms of a Herxheimer reaction developed Several others showed evidence of therapeutic shock by a rise in temperature shortly after penicillin therapy had been instituted It is certain that penicillin causes this reaction in the central nervous system much more commonly than does any other antisyphilitic remedy This is probably due to the ability of penicillin to act readily on T pallidum in the central nervous system In turn, this ability probably accounts for penicillin's remarkable effect on the serologic and clinical course of neurosyphilis

In this series of patients an attempt was made to give each person fifty hours of artificial fever as well as the penicillin therapy This amount is empiric, and it is probable that the benefit of fever can be obtained by fewer treatments It may be necessary to administer the artificial fever only during the time the patient is receiving penicillin

SUMMARY AND CONCLUSIONS

Eighty-seven patients with various forms of neurosyphilis were treated with penicillin combined with artificial fever therapy

Penicillin was administered in two forms (*a*) aqueous penicillin sodium, intramuscularly, every three hours around the clock over a fourteen-day period, for a total dose of 4,500,000 units, and (*b*) penicillin calcium suspended in peanut oil containing 4 5 per cent white wax U S P , administered in daily single intramuscular injections of 300,000 units each for twenty days, for a total of 6,000,000 units

Artificial fever therapy was administered by the blanket method during and subsequent to the penicillin course Five hours of a temperature over 40 C (104 F) was considered a single treatment Most of the patients received a total of fifty hours of fever therapy

The data on 55 of the patients treated are presented Twenty-five of these patients had clinical and serologic evidence of paresis Fifty-five were observed for from 120 to 365 days, 23 were observed for longer periods, and a few were in their third year of post-treatment observation at the time of writing

The clinical response in the patients with dementia paralytica and meningovascular neurosyphilis was satisfactory Little change in the clinical condition was noted in those with tabes dorsalis

The response in regard to spinal fluid abnormalities was excellent Definite improvement in the spinal fluid signs was noted in 70 per cent of the patients during the first year of post-treatment observation and in 87 per cent of those observed for a longer period

taneously the percentage of patients with inactive spinal fluids (grades 1 and 2) increased during the first year of observation, i e, from 42 6 per cent to 90 7 per cent During the second year of observation (of only 23 cases) 82 8 per cent of the patients had inactive spinal fluids Another interesting finding was the increase in the number of normal spinal fluids after treatment Before treatment none of the patients had normal fluids, within one year after treatment 5 (of 53 patients), or 9 3 per cent, had normal fluids, and during the second year of observation 9 (of 23 patients), or 38 7 per cent, had completely normal

TABLE 3—*Changes in Grades of Patterns of Spinal Fluid*

Grade to Grade	120 to 365 Days After Treatment	365 Days + After Treatment
3 to 3	4	3
3 to 2	15	3
3 to 1	11	6
3 to 0	0	5
2 to 2	9	0
2 to 1	6	2
2 to 0	2	3
1 to 1	3	0
1 to 0	3	1
Total	53	23

TABLE 4—*Degree of Change in Spinal Fluid Findings*

Period of Observation	No Change	Improved	Improved Decidedly	Became Worse	Total No of Patients
120 to 365 days	16 (30 1%)	6 (11 3%)	31 (58 6%)	0	53
365 days +	3 (13 0%)	2 (8 7%)	18 (78 3%)	0	23

spinal fluids This observation supports the findings of others that improvement in spinal fluid abnormalities, once obtained, tends to persist and to increase There were instances in which the spinal fluid abnormalities increased after a temporary improvement

Tables 2 and 3 show the changes in the spinal fluid patterns Of the group of patients who had grade 3 spinal fluids before treatment was instituted, 5 continued to show a grade 3 pattern during the first year of observation and 4 still had this pattern during the second year of observation, in spite of repeated courses of treatment There were no significant differences in therapeutic effects noted between the group which received aqueous penicillin sodium and the one which received penicillin in oil and wax Table 4 shows the observations of over-all changes in the spinal fluid

of follow-up for evaluation at this time, although they are all showing a satisfactory trend Only 1 patient has had a second relapse, with the need for additional retreatment The excellent results reported by Dattner and Thomas would indicate that fever therapy may not be required Even if the addition of fever should cause a prompter or earlier improvement of the spinal fluid findings, the end results over long periods of time seem to indicate that treatment with penicillin alone is as effective as and of course much safer than penicillin and fever therapy Although Epstein and Key had to discontinue fever therapy in only 2 patients because of respiratory difficulties and repeated attacks of nausea and vomiting, serious and even fatal untoward reactions associated with other forms of induced fever therapy may occur in from 5 to 20 per cent of patients Furthermore, the cost of hospitalization and nursing care, as well as time lost from employment, especially by the asymptomatic group, must also be considered

It is well known that fever alone is effective on the clinical course and spinal fluid abnormalities of neurosyphilis It has been established, in experimental syphilis, that increase in temperature either in vitro or in vivo enhances the spirocheticidal property of penicillin Considering the excellent reports made by Dattner and Thomas and by Curtis, it is doubtful whether the addition of fever therapy to the administration of penicillin is necessary or justified for all patients with neurosyphilis

DR. ARTHUR C CURTIS, Ann Arbor, Mich I enjoyed hearing Dr Epstein's excellent paper Many of those who in 1944 heard Dr Stokes present his first studies [2a] on the use of penicillin in syphilis of the central nervous system were biased in their opinions It was my feeling at the time that malaria therapy would do more than the administration of penicillin and that a combination of both probably would be the best form of therapy Through the cooperation of the National Research Council, my associates and I began two methods of treatment of syphilis of the central nervous system, which we have continued to date (Curtis, A C , Burns, R. E , and Norton, D H Neurosyphilis Treatment with Penicillin Alone and with a Combination of Penicillin and Malaria, *Am J Syph, Gonor & Ven Dis* **31** 618-632 [Nov] 1947)

One regimen consisted in the administration of penicillin alone in total doses of 4,000,000 units, over a period of twelve and one-half days In the other method the penicillin dose was the same but, in addition, eight to twelve febrile episodes induced by malaria were given

In 750 patients treated since 1945, the over-all results in all types of syphilis of the central nervous system show that treatment with malaria and penicillin combined does little more than the administration of penicillin alone, except to increase the mortality rate In the group which had both therapeutic malaria and treatment with penicillin, improvement in the spinal fluid findings was more rapid, but the net result after two years' observation was no better In a group of more than 100 patients with dementia paralytica and its tabetic form, combined penicillin-malaria therapy seemed to be slightly better than treatment with penicillin alone after two years' observation It is too early to predict what the eventual outcome will be in this group

DR JOSEPH V KLAUDER, Philadelphia It may not be too much digression to take this opportunity to make a plea for the early diagnosis of optic atrophy Among 397 patients with syphilitic primary optic atrophy at Wills Hospital 61 per cent when first seen were industrially blind (had visual acuity with correction of less than 6/60) Diagnosis of optic atrophy is usually made at the time of impaired visual acuity To facilitate early diagnosis routine ophthalmologic

we[15] had used in the past It was not uncommon to observe grade 3 colloidal gold reactions flatten out to a row of zeros The colloidal gold curve reversed to normal in 50 per cent of the cases during the first year of observation and in 70 per cent during the second year of observation The colloidal gold curve was normal in 15 2 per cent of the cases before treatment was given

Tables 6 and 7 show the changes in the colloidal gold reactions as a result of therapy The distinctly abnormal colloidal gold curve, such as 5555432100, is designated as grade 3, a less intense reaction, as grade 2, and one with minimal changes, as grade 1

CHANGES IN THE WASSERMANN REACTION OF THE SPINAL FLUID

The titer of the spinal fluid in the Wassermann test responded less satisfactory to the treatment than did other elements of the spinal fluid. The tendency of the Wassermann reactions to reverse to normal

TABLE 8—*Changes in the Wassermann Reaction of the Spinal Fluid*

Period of Observation	No Change	Decreased	Decreased to Normal	Increased	Total
120 to 365 days	23 (45%)	23 (45%)	4 (8 0%)	1 (2%)	51
365 days +	6 (29%)	8 (38%)	7 (32 4%)	0	21

TABLE 9—*Changes in Serologic Titer of the Blood*

Period of Observation	No Change	Decreased	Returned to Normal	Increased	Total
120 to 365 days	15 (31 4%)	24 (50%)	7 (14 5%)	2 (4 1%)	48
365 days +	6 (28 2%)	10 (47%)	3 (14 1%)	2 (9 4%)	21

increased as the period of observation was lengthened, i e, they became normal in 8 per cent of the cases in the first year and in 32 4 per cent in the second year Table 8 shows these observations

CHANGES OBSERVED IN SEROLOGIC TESTS OF THE BLOOD

Although a decrease in serologic titer was noted in 64 5 per cent of the cases during the first year of observation, in only 14 5 per cent did the titer return to normal Longer observation did not affect these percentages

REACTION TO TREATMENT

The most serious reaction noted was a severe Herxheimer reaction in a white man aged 43, who had dementia paralytica He had been receiving penicillin sodium, 20,000 units every three hours around the clock for thirty-six hours, when the reaction occurred He had

15 Epstein, N N Artificial Fever as an Adjunct in the Treatment of Neurosyphilis, Arch Dermat & Syph **37** 254-266 (Feb) 1938

PARALYSIS OF CRANIAL NERVES COMPLICATING HERPES ZOSTER

MAURICE J COSTELLO, M D
AND
MICHAEL J SCOTT, M D
NEW YORK

HERPES zoster is presumed to be caused by a filtrable virus similar to, if not identical with, that causing varicella This virus is capable of producing an acute inflammatory process in cranial or spinal nerves, ganglions, dorsal and ventral spinal nerve roots, posterior gray matter of the spinal cord or the adjacent meninges, and the disease may therefore be appropriately termed a neuroganglioradiculomeningomyelitis Clinical manifestations consist of a cutaneous grouped vesicular eruption on an erythematous base, neuralgia and, occasionally, paralysis

Many predisposing factors have been suggested as favoring the establishment of herpes zoster seasonal variations, trauma, arsenical drugs, dental pathologic changes, spondylitis, dyscrasias of the blood, including leukemia, Hodgkin's disease and lymphosarcoma, malignant visceral tumors, and tabes dorsalis Sex is not a factor, and herpes zoster has been reported in all age groups, although it occurs most frequently in middle-aged or elderly persons Statistical proof that herpes zoster is commoner in connection with Hodgkin's disease, lymphosarcoma and leukemia is wanting, although clinically it is believed that it is Herpes zoster when a concomitant manifestation of the various types of leukemia occurs most frequently in middle-aged men with lymphatic leukemia, and in such cases the lesions are often of the generalized type [1]

Usually herpes zoster is a benign infection affecting principally the sensory portion of the nervous system Although the severity and duration vary, the course is self limited, terminating usually without sequelae in a few weeks In exceptional cases severe pain persists for

From the Department of Dermatology and Syphilology, New York University College of Medicine, and the Department of Dermatology and Syphilology, Third Medical (New York University) Division, Bellevue Hospital, service of Dr Frank Combes

1 Wile, U J, and Holman, H H Generalized Herpes Zoster Associated with Leukemia, Arch Dermat & Syph **42** 587-592 (Oct) 1940

tion of courses of therapy, is improvement in 70 per cent of the patients treated This, of course, is far better than any that could be accomplished with any other single therapeutic procedure It is evident, in spite of the remarkable effects thus far observed with the penicillin therapy of neurosyphilis, that this therapy has its limitations This fact is further substantiated by observation of patients who are not benefited either clinically or serologically by the administration of penicillin and those who suffer relapses after temporary benefit

These findings have an important bearing on the problem of whether or not the combination of artificial fever therapy and the administration of penicillin offers more to the patient with neurosyphilis than does penicillin alone

If one may judge from the experimental and clinical data already referred to, it would seem logical that the administration of penicillin combined with artificial fever therapy should give therapeutic results superior to those obtained with either alone In the small series of patients reported here, the over-all percentage of improvement obtained during the first year of observation was about 70 per cent During the second year of observation this percentage rose to 87 per cent These findings are of more significance when the fact that approximately one half of our patients had dementia paralytica is taken into consideration

The case of S S, a white woman aged 43 with early dementia paralytica, illustrates the effectiveness of artificial fever therapy after treatment with penicillin apparently had failed to improve her spinal fluid abnormalities and subjective symptoms In April 1946 she received 4,500,000 units of penicillin sodium On Sept 5, 1946, her spinal fluid showed 91 cells (lymphocytes), 88 mg of protein per hundred cubic centimeters, a colloidal gold curve of 555444332 and a strongly positive Wassermann reaction Between Nov 29, 1946 and Jan 29, 1947, the patient received ten weekly pyrexial treatments On May 5, 1947, the spinal fluid showed 4 lymphocytes, a trace of globulin, a colloidal gold curve of 0000000000 and a Wassermann reaction of 4 units This improvement was maintained when the spinal fluid was reexamined four months later

The Herxheimer reactions in the central nervous system which have been noted during penicillin therapy are important, not only from the standpoint of injury to the patient, but also because they possibly indicate a special capacity of penicillin to destroy T pallidum in the central nervous system

Callaway [5] was the first to point out the common occurrence of this reaction in the central nervous system He found that 16 per cent of patients with neurosyphilis had Herxheimer reactions during penicillin therapy Curtis and others [16] observed that this reaction is not

16 Curtis,[7] Stokes, Steiger and Gammon,[2d] Tucker, H A, and Robinson, R C V Neurosyphilitic Patients Treated with Penicillin Probable Herxheimer Reactions, J A M A **132**:281-283 (Oct 5) 1946

17 Footnote deleted on proof

ing motor palsies associated with herpes zoster, irrespective of whether the localization of the eruption is remote or in the vicinity of the paralysis Many cases of the so-called Hunt syndrome in reality probably involve two or more nerves, rather than the seventh cranial nerve alone Herpes zoster occipitocollaris limited to the dermatomes of the second and third cervical nerves depends on connecting tracts existing between these nerves and the seventh cranial nerve in producing a facial paralysis Oculomotor nerves of the eye (third, fourth and sixth cranial nerves) may be involved in the course of zoster of remote localization [5] So, also, in the case reports to follow, are intimate neural circuits seen to be of prime importance in an endeavor to associate and



Fig 1 (case 1) —A photograph taken shortly after the patient's first admission, showing zosteric involvement of the left maxillary dermatome associated with purulent exudate from the left eye Ability to approximate the left eyelids and the presence of wrinkles testified to the absence of a peripheral facial paralysis at that time

explain zosteric involvement of the sensory distribution of one nerve and the subsequent motor paralysis of another cranial nerve

REPORT OF CASES

CASE 1 —*Herpes zoster maxillaris (second division of the trigeminal nerve) with facial paralysis*

O J, a 70 year old Negro, was admitted to the dermatologic wards of Bellevue Hospital on Nov 22, 1947, at which time he complained of swelling of the left cheek and eyelids, of five days' duration, and of slight dizziness Pain had not been present at any time during the course of his illness His past history was irrelevant except for pneumonia in 1917 and hospitalization

5 Edgerton, A E Herpes Zoster Ophthalmicus Report of Cases and Review of Literature, Arch Ophth **34** 40-62 (July), 114-153 (Aug) 1945

The cell count, protein content and colloidal gold reaction of the spinal fluid had a tendency to reverse to normal promptly The Wassermann reaction did not respond as satisfactorily

The reactions to serologic tests of the blood became negative in only 14 5 per cent of the patients during the first year of observation This percentage did not change during the second year of observation

Two severe Herxheimer reactions in the central nervous system were observed A rise in temperature during the first twenty-four hours of aqueous penicillin sodium therapy was noted in 14 of 28 patients so treated

The fever therapy was well tolerated by all but 2 patients

The combination of penicillin and fever therapy gave better effects in our hands than did chemotherapy combined with fever therapy

Penicillin therapy of neurosyphilis, although superior to any other single therapeutic procedure, has its limitations

The effects of artificial fever combined with penicillin therapy should continue to be investigated because of (1) the known effects of artificial fever on the clinical course and spinal fluid abnormalities of neurosyphilis and (2) the experimental data which indicate that elevation of temperature in vitro and in vivo enhances the spirocheticidal properities of penicillin

ABSTRACT OF DISCUSSION

DR CHARLES R REIN, New York Dr Epstein and Dr Key are to be congratulated for their fine report on the treatment of neurosyphilis with penicillin combined with artificial fever induced by the blanket method They are of the opinion that the combination of penicillin and fever therapy gave better effects than did chemotherapy combined with fever treatment Moore, Rose and O'Leary also recommended the combination of penicillin and fever therapy, whereas Curtis showed that penicillin was as effective in the treatment of neurosyphilis when used alone as when combined with fever therapy

Stokes found that the best therapeutic response that one could expect to obtain from the administration of penicillin alone, regardless of dosage and repetition of courses of therapy, is improvement of 70 per cent of patients treated Although this is better than that which could be achieved by any other single therapeutic procedure, Epstein and Key have expressed the opinion that the addition of fever therapy might give results superior to those achieved with either penicillin or fever alone The belief was stated by Dattner and Thomas that the fever therapy is not necessary Since April 1944 they have treated approximately 400 patients at Bellevue Hospital with various forms of neurosyphilis exclusively with intramuscular injections of penicillin Of these persons, 301 received 2,000,000 to 6,000,000 units of penicillin and have been followed for from six to forty-five months The evaluation of therapy in their group was based almost entirely on the results of repeated examination of the spinal fluid There were thirty-four failures of treatment (11 3 per cent) following a single course of varying doses of penicillin However, of the 34 patients for whom treatment was listed as having failed, 19 responded favorably to a second course of treatment with larger doses of penicillin The remaining 15 patients have not yet had adequate periods

five or six days' duration, and also of swelling and pain over the lateral aspect of the left side of his neck since the morning of his second admission He also complained of slight dizziness

Physical examination revealed secondary infection on the left side of the nose and the upper lip, with healing in the areas initially involved No herpetic lesions were noted on the tympanic membrane, the external auditory meatus or in the region of the left ear An inflamed, tender, nonfluctuant mass about 7 or 8 cm in width was present on the left lateral aspect of the neck not involving the mastoid region A complete, hence peripheral, paralysis was present over the left side of the forehead and face (fig 3) Because of the ectropion and partially because of the paralysis, the patient was unable to close his left eye The opening power of both upper lids was unimpaired, as would be expected, since this ability is controlled by the third cranial nerve The corneal reflex was absent on the left side, but the consensual corneal reflex was present, showing damage to the seventh



Fig 3 (case 1) —A photograph of the patient at the time of his second admission (thirty-five days after the onset of the cutaneous eruption) in which flaccid paralysis of the left side of his face may be seen Note the obvious inability of the patient to wrinkle his forehead or to show his teeth on the involved side The ectropion is clearly visible

cranial nerve but not to any sensory portion (ciliary nerves) of the fifth cranial nerve There was no sensory impairment in the region of the ophthalmic or the mandibular division of the trigeminal nerve, but the senses of pain, touch and temperature were absent in the area innervated by the maxillary division on the left side The muscles of mastication were unaffected Sensation of taste on the anterolateral aspect of the left side of the tongue was apparently unimpaired, this finding indicating that the chorda tympani nerve was not involved The Romberg and other neurologic signs were absent The blood pressure was 118 systolic and 54 diastolic Electrical testing showed no reaction of degeneration

On the fourth hospital day the cervical mass, then fluctuant, was incised, and a small lobulation of pus and necrotic tissue was removed On culture hemolytic streptococci were obtained Consultation confirmed our opinion that the abscess

examination should be conducted on all patients with neurosyphilis (Klauder, J V, Meyer, G P, and Gross, B A Syphilitic Primary Optic Atrophy as a Cause of Blindness Importance of Early Diagnosis, *Am J Syph, Gonor & Ven Dis* **32** 574-586 [Nov] 1948)

Dr John Rauschkolb, Cleveland One must take into consideration that syphilis of the central nervous system is a variable process Generally, it starts with inflammatory changes and terminates with degenerative changes Parenchymatous degeneration is almost always preceded by inflammatory processes Physicians are well aware of the fact that arsenical compounds and preparations of the heavy metals are excellent drugs to use in overcoming these early inflammatory changes As the process becomes more chronic and degenerative, pyrotherapy, be it either externally and artifically produced fever or internally produced foreign protein or malarial therapy, has been the method of choice Penicillin probably acts therapeutically more on the inflammatory changes of the central nervous system than on the degenerative changes It has all the excellent qualities of chemotherapy, with minimal toxicity

At Cleveland City Hospital, when possible, a combination of treatment with penicillin and fever therapy in the form of therapeutic malaria is still used to combat the various stages of syphilis of the central nervous system With this combination of therapy it is hoped that the inflammatory changes will be eradicated by administration of penicillin and that the progress of the degenerative changes will be prevented by malaria therapy

Dr Norman Epstein, San Francisco Time does not permit me to present more details of the paper nor to give credit to the many men here who have contributed to this subject Dr Rein summarized the problem very well Do we need fever therapy, or can we do without it? Shall we discard fever therapy, and will penicillin solve the problem alone? If we agree that there are some patients whom penicillin therapy does not cure or even help, then we should not discard other methods of known value That is my feeling in this matter In the present state of knowledge I believe that fever therapy should not be withheld from a patient with signs and symptoms of dementia paralytica Fever therapy should be combined with the administration of penicillin, also, in cases in which treatment with penicillin alone has failed to give a satisfactory therapeutic result

In patients in whom degenerative processes are occurring in the central nervous system time is an important element The sooner the processes are arrested, the better the outlook will be for the patient Fever therapy tends to arrest these degenerative changes much faster than does treatment with penicillin

I wish to thank the discussants for their excellent comments

Pathologic Report on Surgical Specimen (Dec 14, 1948).—The section consisted of a lymph node. There were present large spaces filled with red blood cells, polymorphonuclear leukocytes, a small number of eosinophils and mononuclear cells and, in some areas, a large number of foam cells. These spaces appeared to be enormously dilated vascular channels, and in some of them there were large amounts of coagulated fibrin suggestive of thrombosis. The red cells which were not hemolyzed were sickled. At the margin of the section there was an inflammatory reaction characterized by young granulation tissue, polymorphonuclear leukocytes, mononuclear cells and foam cells. Elsewhere within the structure there was mild hyperplasia of the reticulum cells of the sinuses. Bismarck brown stain failed to reveal the presence of an appreciable number of organisms. The Van Gieson stain for elastin failed to reveal any elastic fibers in the walls of the dilated channels previously described or in the walls of the other veins. The pathologic diagnosis was sicklemia and acute lymphadenitis, with formation of an abscess.

CASE 2.—*Herpes zoster maxillaris with facial paralysis.*

H. R., an 80 year old white man, was admitted to Bellevue Hospital on Dec. 7, 1947, with a painless eruption over the right cheek, of one week's duration. The past history was noncontributory.

An extensive vesicular eruption on an inflammatory base was present over the right maxillary dermatome of the trigeminal nerve. A few aberrant vesicles were also present on the lateral aspect of the right side of the patient's forehead. Eroded vesicles were also observed on the hard and soft palate and on the buccal mucosa, limited to the right side. The right palpebral fissure was closed as a result of periorbital edema. The right conjunctiva was injected, but the cornea was not involved. Sensations of touch, temperature and pain were absent over the area of herpetic involvement on the right cheek. No herpetic lesions or other pathologic changes were found in the auricular or periauricular areas or on the neck or the tympanic membrane. The rectal temperature on the patient's admission was 101.4 F.

Bearing in mind the facial palsy in case 1 and noting the similarity of the signs and symptoms in these 2 cases, we deemed it advisable to follow this patient in the hospital for possible motor complications. Unfortunately for the patient, the vigil was rewarded, as on the twenty-first day of hospitalization a peripheral facial paralysis developed. Neurologic signs characterizing this phenomenon were present, and, as in the first case, the sensory fibers of taste were apparently not affected. Therapy consisted of penicillin, 40,000 units every three hours for a total of seventy doses to control secondary infection, thiamine hydrochloride intramuscularly, and instillations of zinc sulfate into the eye. This patient also showed progressive improvement of the paralysis, with gradual and complete return of muscle power within a six month period.

The laboratory data on the blood on December 8 were as follows: erythrocytes, 5,940,000; hemoglobin, 16.5 Gm.; leukocytes, 6,050, with 60 per cent polymorphonuclear cells, 35 per cent lymphocytes and 5 per cent mononuclear cells. Serologic reactions for syphilis were negative.

NEUROLOGIC ASPECTS

Despite the importance of knowledge concerning the various neural pathways connecting the cranial and cervical nerves in an understanding of the numerous combinations of herpes zoster and paralysis which are likely to occur in the head, such a neurologic discussion would be beyond

years This is especially true of elderly persons Motor symptoms occur infrequently, although both upper and lower motor neuron paralysis complicating herpes zoster has been recorded Of the paralysis of the lower motor neurons facial paralysis associated with otalgia following otic herpes zoster is the commonest J Ramsay Hunt, whose name is synonymous with this syndrome, originally described several such cases in 1907[2] The next most frequently reported palsy is oculomotor muscular paralysis complicating herpes zoster involving the ophthalmic division of the fifth cranial nerve Motor disturbances of the trunk and of the upper and lower extremities less common[3]

Hunt described the following variations of geniculate herpes zoster involving the seventh cranial nerve (1) herpes zoster oticus, (2) herpes zoster oticus with facial paralysis, (3) herpes zoster oticus with facial paralysis and hypacusis and (4) herpes zoster oticus with facial paralysis and Ménière's syndrome Because of their intimate connections Hunt stated the opinion that the ganglions of the fifth, seventh, eighth, ninth and tenth cranial nerves and of the second, third and fourth cervical nerves represent a continuous ganglionic series, all parts having the same embryonal origin in the neural ridge He therefore recognized the possible involvement of cranial ganglions other than the geniculate, but he expressed the belief that such involvement was always secondary to geniculate ganglionitis and never an independently existing infection Hunt stressed the necessity of a ganglionitis and expressed disagreement with the contention that zoster could spread by extension along nerve roots Pathologic investigations have proved this assumption invalid[4] A ganglionitis need not always be present It has also been demonstrated that secondary degeneration may be located in the meninges, the posterior columns of the spinal cord, the spinal nerve roots and the fibers of peripheral nerves

To comprehend clearly the varied manifestations of herpes zoster, especially in regard to the head and neck, it is necessary for one to realize that the presence of herpes zoster in any dermatome denotes not only an infection of the particular neural structures supplying that zone but also the possibility of an ascending or descending neuritis involving the structures of one or more nerves whose pathways connect with the originally infected nerve These connections may be utilized in explain-

2 Hunt, J R On Herpetic Inflammations of the Geniculate Ganglion, J Nerv & Ment Dis **34** 73, 1907

3 Taterka, J H, and O'Sullivan, M E The Motor Complications of Herpes Zoster, J A M A **122** 737-739 (July 10) 1943

4 Denny-Brown, D, Adams, R, and Fitzgerald, P Pathologic Features of Herpes Zoster Note on "Geniculate Herpes," Arch Neurol & Psychiat **51** 216-231 (March) 1944

The trigeminal nerve has three main divisions ophthalmic, maxillary and mandibular (fig 5) The first two are wholly sensory, but the mandibular branch also incorporates motor fibers to the muscles of mastication The ophthalmic branch innervates the forehead, the upper eyelid, the cornea, the conjunctiva, the anterolateral aspect of the nose, the mucous membrane of the nasal vestibule and the frontal sinus The maxillary division supplies the upper lip, the lateral and posterior portions of the nose, the cheek, the anterior portion of the temple and the mucous membrane of the nose, the upper jaw, the upper teeth and the roof of the mouth to the palatopharyngeal arch The sensory branch of the mandibular division innervates the lower lip, the chin, the posterior portion of the cheek and temple, the external ear

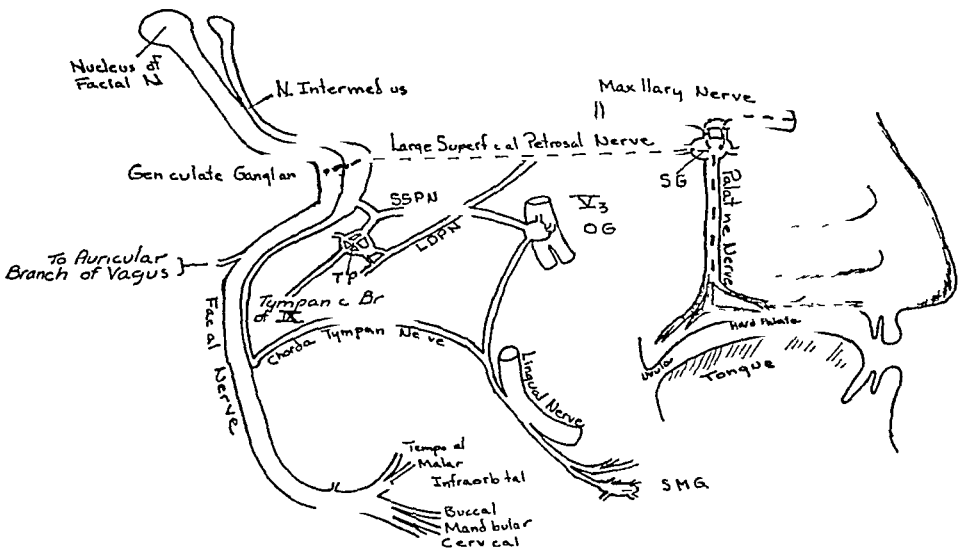


Fig 6—The facial nerve and its communicating branches *O G* signifies the otic ganglion, *S G*, the sphenopalatine ganglion, *S M G*, the submaxillary ganglion, V_3, the mandibular nerve, *SSPN*, the small superficial petrosal nerve, *LDPN*, the large deep petrosal nerve, and *T P*, the tympanic plexus The line of dots and dashes represents the assumed course of infection

and the mucous membrane of the lower jaw, the lower teeth, the cheeks, the anterior two thirds of the tongue and the floor of the mouth All three divisions, together with fibers from the seventh, ninth and tenth cranial nerves, contribute to the sensory innervation of the dura, and these connections are to be remembered when signs of meningitis are present with herpes zoster of the head or neck

The sphenopalatine ganglion is the largest autonomic ganglion associated with the trigeminal nerve and receives a sensory, a motor (parasympathetic) and a sympathetic root derived from the maxillary nerve, the seventh cranial nerve and the carotid plexus, respectively The palatine nerves are distributed to the hard and soft palate, the

of ten days' duration in November 1940 for acute left epididymitis caused by Escherichia coli, which disease had responded to therapy

Examination.—On the patient's admission a vesicular eruption on an erythematous base involved the left side of the nose, the upper lip and the left cheek (fig 1) A few vesicles were present on the left side of the forehead The left periorbital region was swollen and the palpebral fissure nearly closed as the result of the edema The left conjunctiva was inflamed, and a purulent discharge was present Small whitish vesicles, arranged singly and in groups, were observed on the inner aspect of the upper lip, the gingiva, the hard and soft palate, the uvula and the buccal mucosa, sharply limited to the left side of these structures, including the uvula (fig 2) The inner aspect of the left nostril was covered with crusts The other abnormal findings were bilateral submaxillary adenopathy, more evident on the left side, and a reducible right inguinal hernia, vitiligo of the legs and inner aspect of the prepuce was noted The rectal temperature on admission was 104 2 F, and the blood pressure was 134 systolic and 64 diastolic

On the third day after the patient's admission to the hospital the left eyelids were adherent with a purulent exudate The cornea was clear Therapy consisted



Fig 2 (case 1).—Another photograph of O J, also taken shortly after his first admission, illustrating zosteric involvement of the upper lip and the hard and soft palates, limited to the left side of these structures Simultaneous involvement of the hard and soft palates is a rare occurrence, having been recorded on only 4 occasions [10]

of administration of penicillin, 40,000 units every three hours, to combat secondary infection, thiamine hydrochloride, 30 mg three times daily, and nicotinic acid, 50 mg three times daily Compresses soaked in saline solution and ointment containing mercury bichloride were applied for the relief of the ocular symptoms The complement fixation test for syphilis had negative reactions A complete blood count showed these values erythrocytes, 5,380,000, hemoglobin, 14 5 Gm, and leukocytes, 25,250, with 34 per cent polymorphonuclear cells, 62 per cent lymphocytes and 4 per cent mononuclear cells

The course in the hospital was uneventful, and on the thirteenth day after admission the patient was discharged to the outpatient department clinic for treatment of the ectropion which had resulted from cicatrization of the left infraorbital tissues

The patient was readmitted on December 11, seven days after his discharge from the hospital complaining of inability to move the left side of his face, of

tomy on the same side[9] This phenomenon suggests the possibility that pain and hyperesthesia may be mediated by afferent sympathetic nerves (many deny the existence of afferent autonomic cells) or that somatic afferent fibers may also travel by way of the autonomic nervous system Nerve block, since the pathologic change is often proximal to the site of the block, may succeed in relieving only the hyperesthesia, if present, while pain may persist It is interesting to note that, despite the patients' ages and the rather extensive and destructive involvement, pain was conspicuously absent in both case 1 and case 2 This absence, although difficult to explain, may be due to the involvement of both the sensory somatic (maxillary nerve) and the autonomic (sphenopalatine ganglion) neural systems supplying the area involved

CONCLUSIONS

One need only know the established complex neural circuits and the functions of the nerves thereby connected to elaborate numerous theoretically possible syndromes capable of resulting from herpes zoster involving one or more components of these networks It seems reasonable to speculate that, although comparatively few syndromes of the number mathematically possible have been reported, numerous others have occurred but have gone unrecognized With these neural networks in mind it is possible for one to predict various syndromes, which as yet have not occurred or (more probably) have passed unrecognized, in which zosteric involvement of a sensory nerve is followed by motor complications in another nerve Many such cases and syndromes would undoubtedly be discovered through physical and neurologic examinations in all cases of herpes zoster Of particular importance is a follow-up of at least one month in all cases of herpes zoster involving the head and neck, since the neural network is more complex in this region Failure of adequate follow-up undoubtedly explains the paucity in the literature of reports of motor complications resulting from zosteric inflammation of two or more nerves Continued observation is essential because the eruption and paralysis never occur simultaneously and the period of latency may be as long as one month or slightly longer

Any idiopathic facial or other muscular paralysis subsequent to or shortly preceding a herpes zoster eruption of the head should be considered a possible complication of the herpes zoster, and the probable neurologic route of infection should be studied There is no correlation between the severity of the cutaneous eruption and the presence or absence of motor complications of the involved or other nerves

9 Hyndman O R Post-Herpetic Neuralgia in the Distribution of the Cranial Nerves Arch Neurol & Psychiat 42 224-232 (Aug) 1939

had no relation to the preceding facial paralysis Progressive improvement of the paralysis, with gradual return of muscle power, was noted Following his hospital discharge the patient failed to attend the hematology clinic for further investigation to rule out the presence of any possible blood dyscrasia No residuum of the paralysis was present when the patient was observed six months after the onset of his herpetic eruption (fig 4)

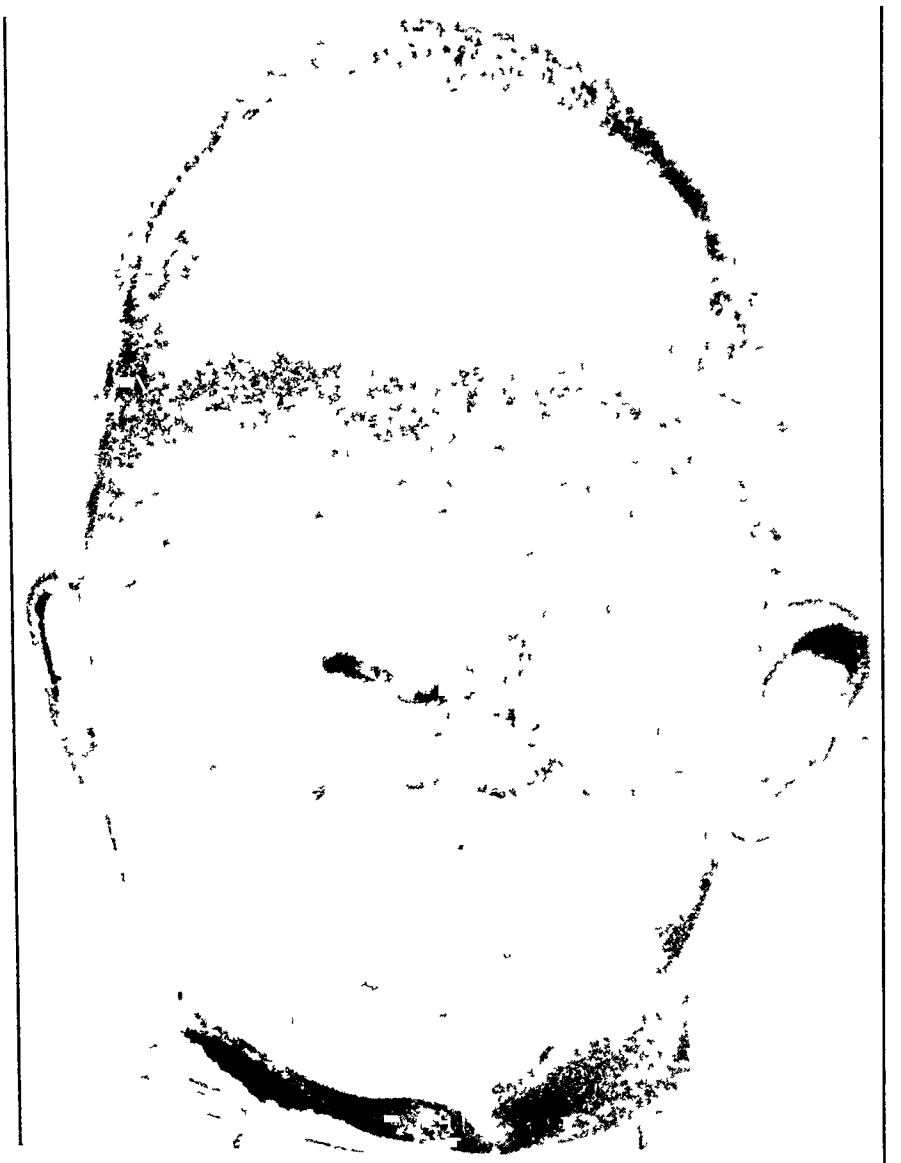


Fig 4 (case 1) —O J , six months after the onset of the herpes zoster eruption Cicatricial deformity is present in the involved region No residuum of the facial paralysis is present

Laboratory examination of the blood produced the following observations

Dec 12, 1947	
Erythrocytes	4,510,000
Hemoglobin	10 5 Gm
Leukocytes	22,850
Polymorphonuclear cells	28%
Lymphocytes	72%

Dec 22, 1947	
Erythrocytes	4,590,000
Hemoglobin	13 5 Gm
Leukocytes	23,750
Polymorphonuclear cells	32%
Lymphocytes	64%
Mononuclear cells	1%
Basophils	2%

Jan 5, 1948	
Erythrocytes	4,010,000
Hemoglobin	11 5 Gm
Differential Count	
Polymorphonuclear cells	29%
Lymphocytes	70%
Basophils	1%

No sickling was noted on the blood smear

RELAPSING FEBRILE NODULAR PANNICULITIS (WEBER-CHRISTIAN DISEASE)

Review of the Literature and Report of a Case

WILLIAM L BENDEL Jr, M D *
NEW ORLEANS

RELAPSING febrile nodular panniculitis, or Weber-Christian disease, is characterized by recurring bouts of fever, associated with the appearance of crops of subcutaneous nodules, varying from the size of a pea to several inches in diameter, usually on the thighs and arms and frequently on the abdomen, back and legs These manifestations may remain separate or become, by confluence, indurated areas of subcutaneous fat The nodules, which may be either painless or tender to touch, are frequently erythematous and raised above the surface of the normal skin The pathologic changes appear to be necrosis of the subcutaneous fat, with infiltration by lipophages and eventually fibrosis Over a period of months the nodules may slowly regress, leaving shallow or deep-pitted areas covered by normal skin [1] As a rule, no pathologic changes are observed in the other systems of the body, although death from the disease per se has been reported in 4 cases [2] In a few cases an enlarged spleen and leukopenia have been outstanding features

To date 43 cases of this syndrome have been reported in the literature This figure is slightly in excess of that reported in other recent articles, but it has been arrived at by a careful survey of the literature, several reports having been found that have not been

*Formerly from the Department of Surgery, Mt Carmel Mercy Hospital, Detroit, now Fellow in Surgery, Tulane University of Louisiana School of Medicine

1 Larkin, V de P , DeSanctis, A G, and Margulis, A C Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease) Review of Literature, with Report of a Case, Am J Dis Child **67** 120-125 (Feb) 1944

2 (*a*) Bailey, R J Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease), J A M A **109** 1419-1424 (Oct 30) 1937 (*b*) Friedman, N B Fatal Panniculitis (Including Autopsy), Arch Path **39** 42-46 (Jan) 1945 (*c*) Miller, J L, and Kritzler, R A Nodular Nonsuppurative Panniculitis (Failure of Sulfonamide Therapy), Arch Dermat & Syph **47** 82-96 (Jan) 1943 (*d*) Ungar, H Relapsing Febrile Nodular Inflammation of Adipose Tissue (Weber-Christian Syndrome) Case With Autopsy, J Path & Bact **58** 175-185 (April) 1946

the realm of this article A brief discussion of the tracts involved in the cases under consideration here, namely the fifth (trigeminal) and the seventh (facial) cranial nerves and the sphenopalatine ganglion is nevertheless indicated The trigeminal and facial nerves are related by means of the superficial petrosal nerves, large and small

The facial nerve is both sensory and motor It contains the following fibers (1) efferent fibers to superficial muscles of the face and scalp and the platysma, the stylohyoid, the posterior belly of the digastric and the stapedius, (2) autonomic efferent fibers to the submaxillary and sphenopalatine ganglions, supplying the submaxillary, sublingual and lacrimal glands and the mucous membrane of the nose and the roof of the mouth, (3) afferent fibers of taste from the anterior two thirds of the tongue, and (4) probably a few afferent fibers which,

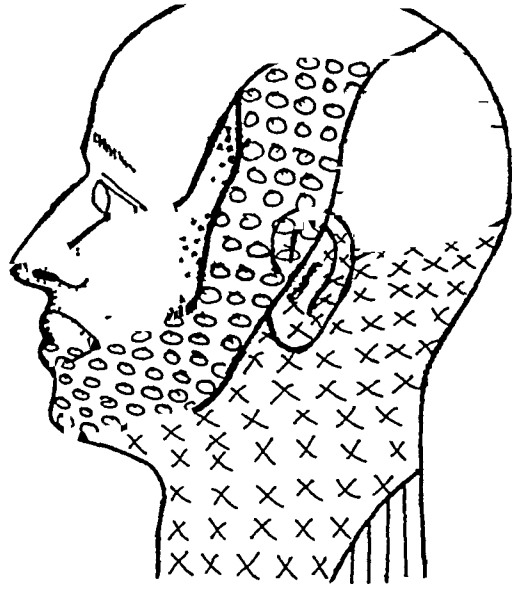


Fig 5—General sensory faciocraniocervical dermatomes The blank area is that supplied by the ophthalmic (V_1) division of the trigeminal nerve, the stippled portion, by the maxillary (V_2) division, the circled area, by the mandibular (V_3) division, the cross hatched part, by the second cervical nerve, the area of crosses, by the third cervical nerve, and the vertically hatched area, by the fourth cervical nerve

together with similar fibers from the ninth and tenth nerves, aid in innervation of the external auditory meatus and the skin back of the ear Although the functional significance of many of the direct branches of communication of the facial nerve, including those with the fifth, eighth, ninth and tenth cranial and cervical nerves, is unknown, each, however, theoretically offers a potential avenue of extension by which an ascending or descending neuritis resulting from herpes zoster could affect other cranial nerves The ramifications of the seventh nerve and also its nucleus receive terminals from many sources, including cranial nerves other than those mentioned above

considered the distinguishing clinical features Bailey [14] in 1937 collected 5 cases from the Mayo Clinic and added them to the literature In 1 of these cases the course was particularly severe, and the patient died, apparently from the syndrome, but permission for necropsy was refused There was either a suspected or a definite history of ingestion of bromides or iodides before onset of the syndrome, or exacerbation of the syndrome occurred after administration of the halide in all these 5 cases Reed and Anderson [15] added the fourteenth case in 1937, followed by Cummins and Lever [16] with 2 cases in 1938, both of which were unusual in that there were striking changes in the walls of the blood vessels in the biopsy sections examined

Shaffer [10c] reported the seventeenth case under the heading of "liquefying nodular panniculitis" and considered his case unique in that the nodules contained a yellowish brown fluid which would eventually rupture to the exterior Binkley [10a] shortly afterward reported a similar case, in a 36 year old woman, in which the cystic masses were first found in the breasts and later spread to the arms and legs Puente's [8b] case, reported in 1938, is included here as the eighteenth, although it, occurring in a woman aged 48, was the only one in which micro-organisms (Staphylococcus aureus) were found in the nodules In Mengoli's case [17] the patient was afflicted while convalescing from typhus Hazel and Lamb [18] in January 1940 reported the case of an 11 year old girl with lesions of the abdomen and legs The lesions clinically resembled those of morphea, or localized scleroderma The patient was afebrile while observed, but otherwise the findings were typical of Weber-Christian disease

Tilden, Gotshalk and Avakian [19] added the twenty-second and twenty-third cases in 1940 In the first of these the patient died of tuberculosis eight and one-half months after having been apparently cured of his panniculitis Permission for necropsy was obtained, but examination revealed nothing significant other than the tuberculosis

14 Bailey, R J Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease), J A M A **109** 1419-1424 (Oct 30) 1937

15 Reed, A C, and Anderson, H H Relapsing Nonsuppurative Panniculitis, California & West Med **47** 325 (Nov) 1937

16 Cummins, L J, and Lever, W F Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease), Arch Dermat & Syph **38** 415-426 (Sept) 1938

17 Mengoli, cited by Baumgartner and Riva [4]

18 Hazel, O G, and Lamb, J Primary Panniculitis Afebrile in Type and Associated with Sclerodermatous-like Changes, J Oklahoma M A **33** 1-5 (Jan) 1940

19 Tilden, I L, Gotshalk, H C, and Avakian, E V Relapsing Febrile Nonsuppurative Panniculitis, Arch Dermat & Syph **41** 681-689 (April) 1940

tonsils, the uvula and the lining membrane of the nasal cavity Most of their fibers are derived from the sphenopalatine branches of the maxillary nerve [6]

In both cases reported there was facial nerve involvement, most likely from initial infection of the maxillary nerve with extension via the sphenopalatine ganglion and the large superior petrosal nerve, as shown in figure 6

THERAPY

The management of herpes zoster is symptomatic Since pain is usually the outstanding complaint, relief is often the main problem of therapy The patient may require only salicylates or codeine, but in extreme cases even morphine may prove unsuccessful Although no medication has been discovered which shortens the course of the disease, many drugs may be used to help comfort the patient Administration of surgical pituitrin® (posterior pituitary solution containing 20 pressor units per cubic centimeter), use of convalescent serum, roentgen therapy, ultraviolet irradiation, diathermy, injection of foreign protein, autohemotherapy and administration of diphtheria antitoxin, thiamine hydrochloride and sodium iodide, among other measures, have all been reported as being helpful in some hands The cutaneous lesions respond best to an occlusive type of dressing, and therefore collodion, paraffin or pliable paraffin (paressine®), for example, are especially useful for topical application Residual scar deformities, such as the ectropion cited in case 1, may be sufficiently extensive to warrant plastic surgery Optic involvement should be treated promptly by an ophthalmologist It is a clinical prognostic sign that ophthalmic complications are more likely to occur if there is involvement of the nasociliary branch of the ophthalmic division of the fifth cranial nerve, clinically manifested by a vesicular eruption over the anterolateral aspect of the nose Following facial paralysis residual motor signs may persist, but nearly complete or total recovery is apparently commonest Faradic current or other types of electrical stimulation may be employed in the treatment of muscular paralysis Nerve block or surgical sectioning of the nerve or its ganglion may be necessary in severe neuralgias, although even the latter procedure is occasionally unsuccessful in the relief of post-herpetic pain in the distribution of the cranial nerves [8] In such cases neuralgia may be eliminated by stellate and upper thoracic ganglionec-

6 Strong O S and Elwyn, A Human Neuroanatomy, Baltimore, Williams & Wilkins Company 1943 Gray, H Anatomy of the Human Body, edited by W H Lewis, ed 24, Philadelphia, Lea & Febiger, 1942

7 Footnote deleted

8 Peet M M Post-Herpetic Trigeminal Neuralgia, J A M A 92 1503-1505 (May 4) 1929

Two more cases were reported by Carol and associates[25] in 1941 Rosenberg and Cohen[26] added 2 more cases to the literature in 1942 and reported that in their cases they had been able to produce the lesions at will with either iodides or bromides once the syndrome had been established

Miller and Kritzler[2c] in 1943 reported the first autopsy on a patient whose death had resulted from Weber-Christian disease They were unable to find any specific lesions internally and gave as nonspecific lesions the accumulation of fat and focal necrosis of the liver, hydropic degeneration of the adrenal cortex cells and the presence of large numbers of red cells in the fixed members of the reticuloendothelial system They emphasized the failure of the sulfonamide compounds (sulfadiazine, sulfathiazole and sulfanilamide) to have a favorable influence on the course of the disease Their patient was a 34 year old Jewish housewife

Larkin and associates[1] reviewed the literature in 1944 and added the case of a 2 year old male child with lesions of the feet and ankles, which were apparently asymptomatic with the exception of the fact that the patient had an undulating fever, with temperatures occasionally as high as 102 F Spain and Toby[27] reported an interesting case in which the patient was admitted to the hospital and died one week later with uremia from the terminal stage of chronic glomerulonephritis During this week nodules which were typical of Weber-Christian disease developed A necropsy was performed, and, besides the expected observations of the effects of the glomerulonephritis, nodules of fat necrosis were found in the panniculus adiposus and in the omental, mesenteric and pretracheal fat deposits This case, then, represented the first one in which specific internal lesions, as well as specific external lesions, were reported

Baumgartner[28] reported the thirty-seventh case in 1944 and the thirty-eighth case[4] in 1945 Friedman[2b] reported the thirty-ninth case of the Weber-Christian syndrome in 1945 and was able to secure an autopsy on the patient The primary cause of death was septicopyemia due to infection with Staphylococcus albus and Staph aureus The pathologic alterations in the viscera yielded no light as to the essential nature of the disease Changes in the visceral adipose tissue, such as those described by Spain and Toby, were not seen Focal lesions in

25 Carol, W L , Prakken, J R , and van Zwijndregt, H A , cited by Baumgartner and Riva[4]

26 Rosenberg, W A , and Cohen, T M Relapsing Febrile Nodular Nonsuppurative Panniculitis, Illinois M J **81** 59-62 (Jan) 1942

27 Spain, D M , and Toby, J M Nonsuppurative Nodular Panniculitis (Weber-Christian Disease), Am J Path **20** 783-787 (July) 1944

28 Baumgartner, W Pathology of Adipose Tissue, Helvet med acta **11** 155-159 (April) 1944

The development of herpes zoster should also suggest the possibility of lymphosarcoma, Hodgkin's disease or leukemia The possible persistence of post-herpes-zoster pain, scar formation, ophthalmic involvement or, occasionally, paralytic complications should be considered when a prognosis is offered

The similarity of the 2 cases reported here consists in the following symptoms and signs (1) herpes zoster of the maxillary division of the fifth cranial (trigeminal) nerve, involving both cutaneous and mucous membrane dermatomes, (2) absence of pain, and (3) ipsilateral peripheral facial paralysis There findings present the possibility of a clinical syndrome Our review of the literature in English revealed no case recorded which exactly paralleled those described above Two interesting cases were reported, however, in which herpes zoster involved the hard and soft palate and nasal mucosa, in addition to being associated with an ipsilateral vesicular auricular eruption, auricular neuralgia and facial palsy [10] The auricular element in these reported cases suggests the possibility of an associated Hunt syndrome

SUMMARY

Two cases of facial paralysis complicating herpes zoster involving the maxillary branch of the fifth (trigeminal) nerve are reported Cutaneous involvement preceded the paralysis by approximately twenty days in case 1 and by twenty-six days in case 2 The similarity of symptoms and signs in both cases is striking

140 East Fifty-Fourth Street (22)

10 Wakeley, C P G, and Mulvany, J H A Rare Feature of the Ramsay Hunt Syndrome, with Some Observations on Sensory System of Seventh Nerve, Lancet **1** 746-750 (April 1) 1939

The following is the forty-fourth case to be reported, in this instance, the syndrome was secondary and incidental to the compliant for which the patient was admitted

REPORT OF CASE

Mrs A J, aged 35, was admitted May 11, 1947, to Mt Carmel Mercy Hospital, Detroit, to the surgical service of Dr William Cassidy, with a complaint of tumor of the right breast She was unsure of the duration, but she had discovered the growth three weeks before admission She had had no pain in the breast at any time In addition to her chief complaint, she stated that she had

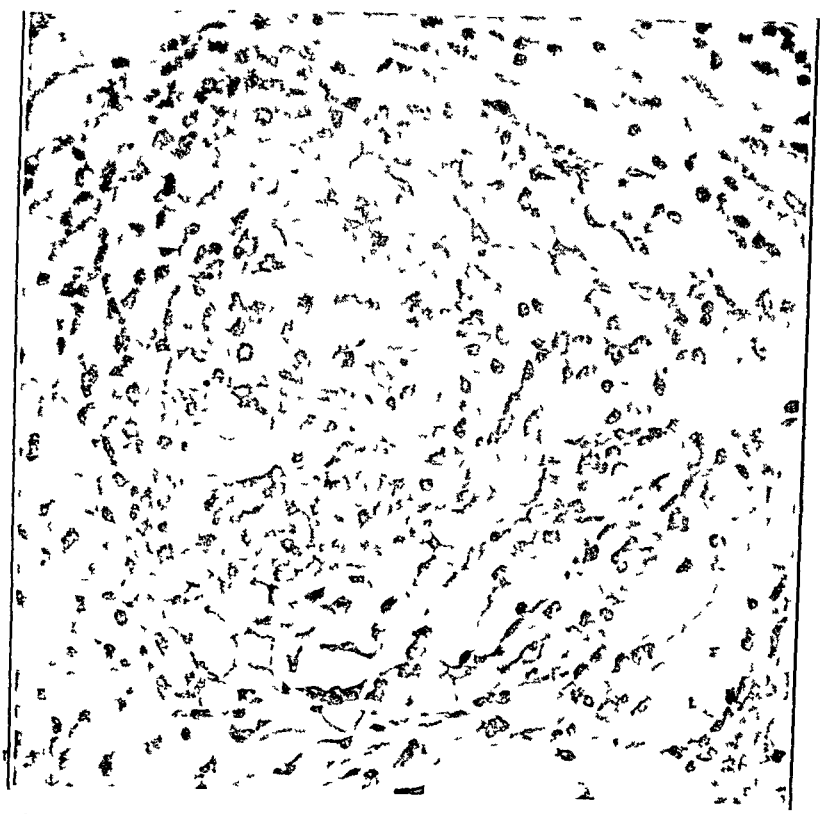


Fig 1—A solitary tubercle-like lesion composed of epithelioid-like cells arranged in a concentric or diffuse manner A typical Langhans giant cell is seen in the upper part of the whorls of the tubercle-like lesion

had multiple painful, bean-sized nodules on her arms and legs, some of which were still present In the acute stage these lesions produced a purplish discoloration of the overlying skin, which finally changed to a brown and then faded nearly completely The nodules were subcutaneous in origin and location, and ulceration had never occurred The patient stated that she had been bothered with the condition for a three year period and that there was a tendency for the lesions to regress in the spring and summer In winter, during an acute attack, the patient had been unable to walk because of swelling of the legs and pain About two years before admission she had been admitted to another hospital and a biopsy of a nodule had been done The biopsy at that time had revealed only

previously included in reviews Of these, 2 cases [3] are not particularly well authenticated but are included because of their inclusion in Baumgartner's series [4]

The first case was described by Pfeifer [5] in 1892, the second, concerning which the authors emphasized the role of the macrophage in the lesion, was reported by Gilchrist and Ketron [6] in 1916 Weber,[7] in reporting the third case in 1925, supplied the name "relapsing nonsuppurative nodular panniculitis," and to this Christian [8] added the adjective "febrile" in reporting the fourth case in 1928 "Nonsuppurative" is not used in this paper because several cases of the syndrome have been reported which fulfil all the criteria with the exception that either frank pus [9] or a greenish yellow mucoid material [10] was to be found in the nodules, albeit the material was in each instance sterile

The fifth and sixth cases were reported by Alderson and Way [11] and Netherton [12] in 1935 Weber,[9b] in reporting the seventh case, suggested iodides as the probable cause in this case, as the onset followed the ingestion of iodides, and a recurrence occurred with a second administraton of them Brill [13] reported the eighth case and summarized what he

3 (*a*) Pinetti, V, cited by Baumgartner and Riva [4] (*b*) Puente, cited by Baumgartner and Riva [4]

4 Baumgartner, W, and Riva, G Nodular Inflammation of Adipose Tissue, Helvet med acta (supp 14) **12** 1-69, 1945

5 Pfeifer, V Ueberwein Fall von herdwein Atrophie des subcutanein Fettgewebes, Arch f klin Med **50** 438-449, 1892

6 Gilchrist, T C, and Ketron, L A Unique Case of Atrophy of the Fatty Layer of the Skin, Preceded by the Ingestion of the Fat by Large Phagocytic Cells—Macrophages, Bull Johns Hopkins Hosp **27** 291-294 (Oct.), 1916

7 Weber, F P A Case of Relapsing Nonsuppurative Nodular Panniculitis, Showing Phagocytosis of Subcutaneous Fat Cells by Macrophages, Brit J Dermat **37** 301-311 (July) 1925

8 Christian, H A Relapsing Febrile Nodular Nonsuppurative Panniculitis, Arch Int Med **42** 338-351 (Sept) 1928

9 (*a*) Ungar [2d] (*b*) Weber, F P A Further Note on Relapsing Febrile Nodular Nonsuppurative Panniculitis, Brit J Dermat **47** 230-233 (June) 1935

10 (*a*) Binkley, J S Relapsing Febrile Nodular Nonsuppurative Panniculitis, J A M A **112** 113-116 (July 8) 1939 (*b*) Ives, G Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease) with Report of Case J Missouri M A **42** 409-410 (July) 1945 (*c*) Shaffer, B Liquefying Nodular Panniculitis, Arch Dermat & Syph **38** 535-544 (Oct) 1938

11 Alderson, H E, and Way, S C Relapsing Febrile Nonsuppurative Panniculitis (Weber), Arch Dermat & Syph **27** 440-449 (March) 1933

12 Netherton, E W Relapsing Nodular Nonsuppurative Panniculitis, Arch Dermat & Syph **28** 258-359 (Aug) 1933

13 Brill, I C Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease) in Medical Papers Dedicated to Henry Asbury Christian in Honor of His Sixtieth Birthday, Baltimore, Waverly Press, Inc, 1936, p 624-704

tive reactions The provisional diagnosis of the tumor in the breast was fibroadenoma or carcinoma, and the provisional diagnosis of the nodules on the legs was erythema nodosum

On May 12, 1947, the patient was taken to the operating room, and, while she was under cyclopropane anesthesia, the mass in the right breast was excised After this operation, one of the subcutaneous nodules from the lower third of each leg was excised and sent to the laboratory for examination The patient made an uneventful recovery after the operation Roentgenologic examination of the thorax revealed some infiltration of all markings, heaviest in the base of the right lung Both paravertebral gutters were clear There were no areas of consolida-

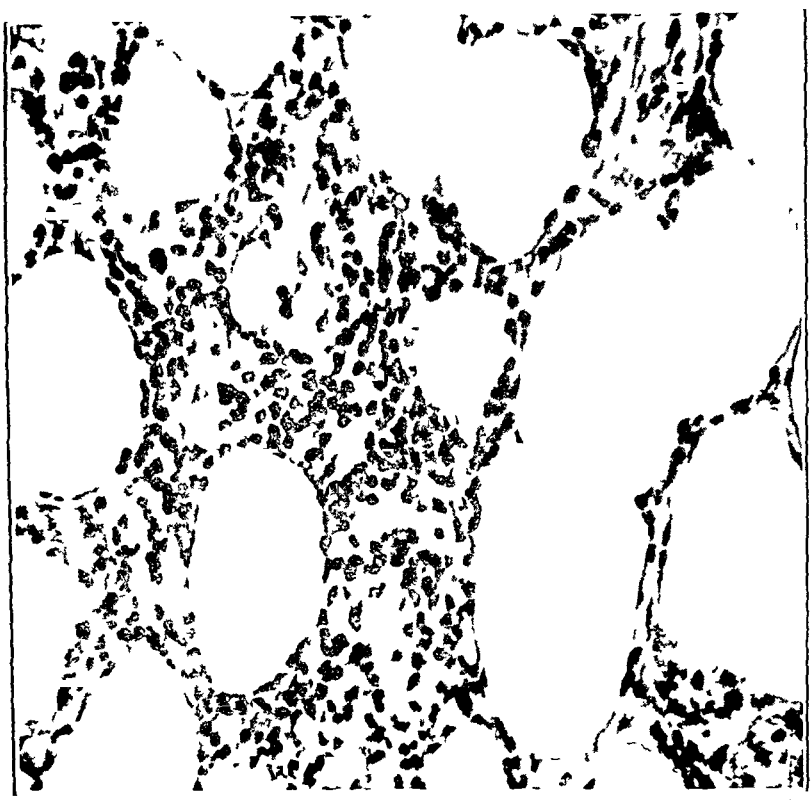


Fig 3 —Cellular infiltration of the fat and connective tissue Numerous small, oval clear spaces remain, corresponding to the remnants of the subcutaneous fat tissue which has not been infiltrated

tion in either pulmonary field There was no evidence of metastasis in either the lungs or the thoracic cage

Dr L W Gardner rendered the following pathologic report

"*Gross Examination*—1 The specimen (tumor of the breast) consisted of a round fragment of tissue measuring 5 5 cm in diameter and 1 5 cm in thickness The tissue was pinkish gray and somewhat rough but glistening The tumor was firm, nonfriable and definitely rubbery *Cross sections* revealed a homogeneous yellowish white fibrous surface which did not grate when cut

"2 In addition, there was an oval mass of tissue measuring 2 5 by 1 cm One surface had attached to it an elliptic fragment of skin Also, there was a mass

Skiold [20] in 1940 described a clinically typical case, the patient being a 51 year old woman with lesions beginning on the lower extremities and a temperature as high as 104 F During the course of a year some of the lesions healed, with depression of the cutaneous surface, but new lesions continued to form A purulent infection of the teeth, necessitating the extraction of fourteen teeth, was accompanied by a distinct increase in the number of new lesions and an elevation of temperature

Hartwell and Thannhauser [21] reported the case of a 32 year old white woman whose lesions began on the shins and soon spread over the back, abdomen, breasts and neck When first observed, she had, in addition to the nodules, acute pericarditis and pleural effusion She had a temperature as high as 103 F Crusting was present over two of the nodules There was gradual improvement, and after six admissions to the hospital the patient had gained 43 pounds (19 5 Kg) No evidence of cardiac change was present, and the nodules had healed, leaving depressed areas

Ziegert [22] in September 1940 reported the case of a 34 year old woman with two palm-sized lesions on the chest and abdomen and smaller lesions in the left axilla and on the arms Fever and leukopenia were present The histologic observations reported conform to those made in other cases of this disease

Hanson and Fowler [23] in 1941 reported the case of a 28 year old white man with recurring lesions on the right leg Their patient showed slow healing of the wound made for removal of a biopsy specimen, as well as the unusual feature of spontaneous rupture of a lesion on the calf

Pinetti, according to Baumgartner and Riva,[4] in 1941 reported the case of a 2 year old male baby who had lesions in the unusual locations of the head, the neck and the penis Larson and Ootkin [24] reported the case of a 58 year old man who was observed with a number of painful nodules on the chest, the back, the thighs and the arms The histologic picture was typical The patient was observed for eight months, during which time there was no recurrence of the disease

20 Skiold, N Relapsing Febrile Nonsuppurative Panniculitis, Acta med Scandinav **105** 43-47, 1940

21 Hartwell, A S, and Thannhauser, S J Case Presentation and Discussion of Relapsing Febrile Nodular Nonsuppurative Panniculitis, Bull New England M Center **2** 362-369 (Dec) 1940

22 Ziegert, H J Febrile Panniculitis (Weber-Christian Disease), Zentralbl f inn Med **61** 610-612 (Sept) 1940

23 Hanson, W A, and Fowler, L H Relapsing Febrile Nodular Nonsuppurative Panniculitis, Minnesota Med **24** 779-782 (Sept) 1941

24 Larson, C P, and Ootkin, B N Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease) Case, Am J Clin Path **11** 781-787 (Oct) 1941

In some sections there was rather dense inflammatory infiltration (fig 4) Beginning fibrosis with gradual invasion by young connective tissue was noted in some sections (fig 5) Special stains for fat revealed the presence of fat within the macrophages The lobular arrangement of the fat appeared to limit partially the process of infiltration and proliferation Stains for acid-fast organisms were negative

The patient, in good condition, was discharged from the hospital on May 16, 1947, the final diagnoses being as follows (1) chronic cystic mastitis, no malignant characteristics, and (2) relapsing febrile nodular panniculitis (Weber-Christian disease), no malignant characteristics

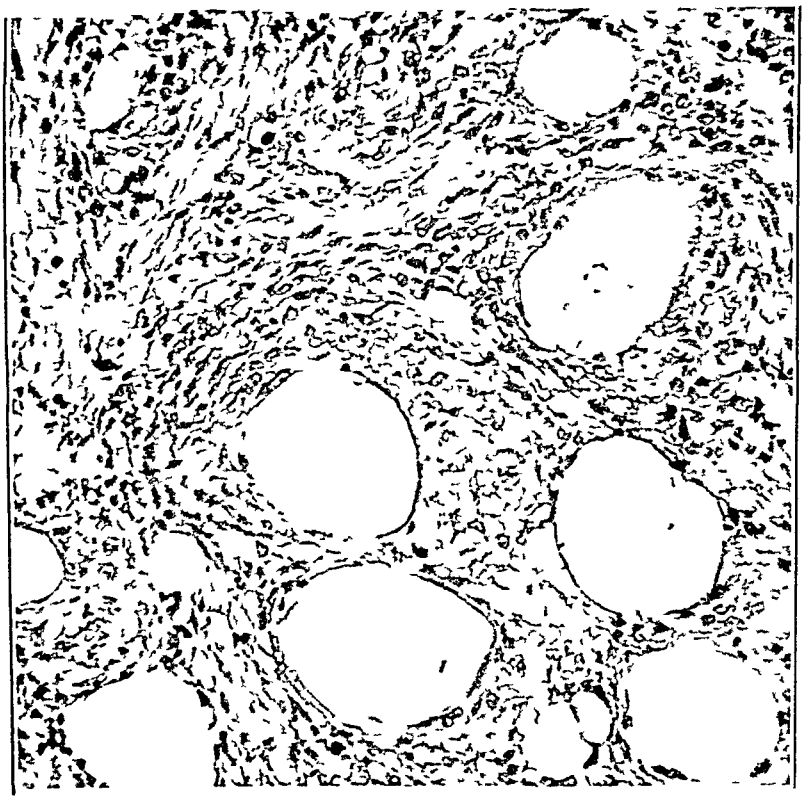


Fig 5—Large fat spaces resulting from coalescence of necrotic fat cells, with beginning infiltration of the inflammatory area and replacement by fibrotic tissue

The outcome in the 44 previously reported cases, then, has been as follows

Six deaths have been reported in connection with the syndrome In Bailey's case the patient died apparently as a result of the syndrome, but no autopsy was permitted In Tilden's case the patient died from tuberculosis after having apparently been cured of the disease, the autopsy having revealed no lesions attributable to the Weber-Christian syndrome The first death from the Weber-Christian syndrome with autopsy reported was that of Miller, who likewise was unable to find any specific internal lesions The patient in Spain and Toby's case died

the adrenal cortex similar to those noted in Miller and Kritzler's case were observed here

Arnold [29] added a report of a case in 1945 in which he described the control of the disease by means of sulfapyridine after sulfathiazole, sulfadiazine and sulfanilamide had all failed He stated that on discontinuance of treatment with sulfapyridine the symptoms would immediately reappear, although in each instance to a less degree, and that on resumption of administration of the drug the symptoms would promptly disappear Arnold found a close correlation in his case between the clinical course and the erythrocyte sedimentation rate and the Weltmann coagulation reaction His patient had five relapses and five remissions, according to whether sulfapyridine was given or not, and finally seemed to have attained a permanent remission without the drug

In 1945 Ives [10b] added the forty-first case, one in which there was a definite antecedent history of an ulcer of the arm from a cigaret burn Ungar [2d] recorded another death from the Weber-Christian syndrome, in a woman aged 37, who died nine months after the onset of her illness Hers was one of the few reported cases in which there was a positive reaction to the serologic test for syphilis It was interesting to note that potassium iodide therapy was attempted and produced an exacerbation of this patient's lesions Ungar entitled his article "Relapsing Febrile Nodular Inflammation of Adipose Tissue," thus giving a hint of the manner in which his case differed from the usual picture presented There was a pronounced tendency toward suppuration of the nodules, this manifestation rendering invalid the adjective "nonsuppurative," usually employed in describing the syndrome Apparently the cause of death in this case was a hematogenous peritonitis, the infection (with hemolytic streptococci) having arisen from the tonsils, which contained abundant streptococcic abscesses Ungar expressed the opinion that the nonsuppurative changes have no specific significance in the pathologic process of the Weber-Christian syndrome and that they are more likely to be due to tissue injury by fatty substances liberated in the course of destruction of fat cells by suppurative inflammation Autopsy revealed granulomatous and suppurative involvement of both the panniculus adiposus and the adipose tissue in the thorax and the abdomen

Zee [30] reported the forty-third case in 1946, that of a man aged 23 who was treated first with sulfadiazine, with no relief, and then with penicillin, with an apparent cure Zee urged further trial of penicillin in the treatment of the syndrome

29 Arnold, H L, Jr Nodular Nonsuppurative Panniculitis (Weber-Christian Disease) Preliminary Report of Case Controlled by Sulfapyridine (Sulfonamide), Arch Dermat & Syph **61** 94-99 (Feb) 1945

30 Zee, M L Nodular Nonsuppurative Panniculitis Treated with Penicillin, J A M A **130** 1219-1220 (April 27) 1946

TABLE 1.—*Summary of Forty-Four Cases of the Weber-Christian Syndrome*

Case No	Author	Duration, Yr	Year	Age, Yr	Sex	Pain	Fever	Distribution: Arms	Abdomen	Back	Thighs
1	Pfeifer [5]	2	1892	23	F	—	+	+	+	+	+
2	Gilchrist and Ketron [6]	½	1916	8	F	—	+	—	—	—	+
3	Weber [7]	1/10	1925	50	F	+	+	+	—	+	±
4	Christian [8]	10	1928	25	F	—	+	+	+	+	—
5	Netherton [12]	1	1933	46	F	+	+	—	—	—	—
6	Alderson and Way [11]	15	1933	41	F	+	+	+	—	—	±
7	Weber [9b]	1/12	1935	53	M	+	+	+	—	—	±
8	Brill [13]	3	1936	19	F	+	+	+	+	—	±
9	Bailey [14*]	⅓	1937	24	F	+	+	+	+	+	±
10	Bailey [14]	¾	1937	43	F	—	+	+	+	—	±
11	Bailey [14]	¾	1937	56	F	+	+	—	+	—	±
12	Bailey [14]	4	1937	38	M	—	+	+	—	—	±
13	Bailey [14]	10	1937	45	F	—	+	+	+	—	±
14	Reed and Anderson [15]	9	1937	34	F	+	—	—	—	—	±
15	Cummins and Lever [16]	⅙	1938	10	F	—	+	+	—	—	—
16	Cummins and Lever [16]	½	1938	10	F	+	+	—	—	—	+
17	Shaffer [10c]	12	1938	33	F	—	+	+	?	?	+
18	Puente [3b]	2½	1938	48	F	+	+	—	—	+	—
19	Binkley [10a]	⅙	1939	36	F	—	—	+	—	—	—
20	Mengoli [17]	½	1939	12	M	+	+	+	—	+	+
21	Hazel and Lamb [18]	1	1940	11	F	—	—	—	+	—	+
22	Tilden, Gotshalk and Avakian [19†]	1/12	1940	64	M	+	+	+	+	+	+
23	Tilden, Gotshalk and Avakian [19]	1/12	1940	54	F	+	+	—	+	—	±
24	Skiold [20]	4	1940	51	F	+	+	+	—	—	±
25	Hartwell and Thannhauser [21]	2	1940	32	F	—	+	+	+	+	—
26	Ziegert [22]	?	1940	34	F	+	+	+	+	+	—
27	Hanson and Fowler [23]	¼	1941	28	M	+	+	—	—	—	—
28	Pinetti [3a]	?	1941	2	M	?	+	+	—	—	+
29	Larson and Ootkin [24]	1/12	1941	58	M	+	+	+	+	+	+
30	Carol, Prakken and van Zwijndregt [25]	?	1941	35	F	?	?	+	—	—	—
31	Carol, Prakken and van Zwijndregt [25]	?	1941	½	F	?	+	+	+	—	±
32	Rosenberg and Cohen [26]	1/12	1942	38	F	+	+	—	—	—	—
33	Rosenberg and Cohen [26]	1/30	1942	35	F	+	—	—	—	—	—
34	Miller and Kritzler [26‡]	5/12	1943	34	F	+	+	+	—	+	±
35	Larkin, DeSanctis and Margulis [1]	¼	1944	2	M	—	+	—	—	—	—
36	Spain and Toby [27§]	1/365	1944	51	M	+	+	+	—	—	—
37	Baumgartner [28]	10	1944	40	F	+	+	+	—	+	+
38	Baumgartner [28]	8	1945	56	F	+	+	+	+	+	±
39	Friedman [2b‖]	1	1945	23	F	+	+	—	—	—	+
40	Arnold [29]	½	1945	27	F	+	+	+	—	+	±
41	Ives [10b]	1/24	1945	53	M	—	+	+	—	—	+
42	Ungar [23¶]	1/12	1946	37	F	+	+	+	+	+	+
43	Zee [30]	1/12	1946	23	F	—	+	+	±	+	±
44	Bendel	1/12	1948	35	F	+	—	+	—	—	—

* Death apparently from Weber Christian disease No autopsy
† Death from tuberculosis, apparent cure of Weber Christian disease Autopsy
‡ Death from Weber Christian disease First reported autopsy

a chronic dermatitis There were no operations or other serious illnesses in her past history Her menstrual periods had been irregular for two and one-half months prior to admission to that hospital, having occurred every nineteen days Before that they had been regular, having occurred every twenty-eight days with a duration of seven days She had one child, full term, born about one month before her present admission She had had a premature delivery at eight months, seventeen months before this admission, the child having lived two and one-half days

Physical examination revealed a well developed and well nourished white woman, not acutely ill The entire physical examination was noncontributory, with the following two exceptions 1 The left breast showed no masses, the right breast revealed an irregular ill defined mass just deep to the nipple, mov-



Fig 2—Several large foam cells, or macrophages ("lipophages")

able, firm, not attached to the skin or overlying fascia and possibly the size of a small lemon, no nodes were palpable in the axillas 2 On the lower third of each leg there were subcutaneous nodules, about the size of olives, although considerably more flattened, these were firm, and slightly movable, with apparently normal overlying skin, several were present on each leg and were slightly tender

A complete blood count revealed no abnormalities hemoglobin, 13 4 Gm , red blood cells, 4,220,000, white blood cells, 7,400, polymorphonuclear leukocytes, 52, lymphocytes, 35, monocytes, 5, basophils, 1, and stab cells, 7 Reactions to the Kahn test were negative, and urinalysis showed normal condition Blood cholesterol was 183 mg per hundred cubic centimeters Tuberculin tests elicited nega-

TABLE 2—*Review of the Laboratory Data on Forty-Four Cas*

Case No	Author	Year	Age, Yr	Blood Count: Red Blood Cells (Millions)	Blood Count: White Blood Cells	Blood Count: Differential	Blood Count: Hemoglobin	Sternal Marrow	Lipids, Mg / 100 Cc	Cholestero Mg / 100 Cc
1	Pfeifer [5]	1892	23	4 1	Normal	Normal	85%			
2	Gilchrist and Ketron [6]	1916	8		15,600	Polymorphonuclear cells				Normal
3	Weber [7]	1925	50	4 4	10,500	Normal	85%			
4	Christian [8]	1928	25	4 9	3,000	Normal	85%			
5	Netherton [12]	1933	46	5 0	6,900	Normal	78%			
6	Alderson and Way [11]	1933	41							
7	Weber [9b]	1935	53							
8	Brill [13]	1936	19		Leukopenia	Lymphocytes		Normal		230
9	Bailey [14]	1937	24	3 9	5,100		54 6%			
10	Bailey [14]	1937	43	4 6	6,900		69%			
11	Bailey [14]	1937	56							
12	Bailey [14]	1937	38							
13	Bailey [14]	1937	45	Normal	Normal	Normal	Normal			
14	Reed and Anderson [15]	1937	34	4 3	6,600	Normal	90%			
15	Cummins and Lever [16]	1938	10	Normal	Normal	Normal	Normal		Normal	Normal
16	Cummins and Lever [16]	1938	10	Normal	11,500	Normal	Normal			
17	Shaffer [10c]	1938	33	Normal	4,000	Normal				125 205
18	Puente [3b]	1938	48	Anemia	5,800	Lymphocytes				
19	Binkley [10a]	1939	36	4 4	13,000	Normal	85%		644	199
20	Mengoli [17]	1939	12							
21	Hazel and Lamb [18]	1940	11	4 5	16,800	4% Eosinophils				190
22	Tilden, Gotshalk and Avakian [19]	1940	64	3 3	6,800	Normal	50%	Normal		117
23	Tilden, Gotshalk and Avakian [19]	1940	54	3 7			56%			151
24	Skiold [20]	1940	51	4 3	3,100	5% Eosinophils	90%			
25	Hartwell and Thannhauser [21]	1940	32							
26	Ziegert [22]	1940	34	Anemia	3,300					
27	Hanson and Fowler [23]	1941	28	Normal	Normal		89%			166 6
28	Pinetti [3a]	1941	2	Normal	Normal	Normal	Normal			
29	Larson and Ootkin [24]	1941	58	Normal	Normal	Normal	Normal			
30	Carol, Prakken and van Zwijndregt [25]	1941	35							
31	Carol, Prakken and van Zwijndregt [25]	1941	½							
32	Rosenberg and Cohen [26]	1942	38	4 4	8,650	Normal	13 2 Gm			334
33	Rosenberg and Cohen [26]	1942	35	4 1	5,750		12 4 Gm			218
34	Miller and Kritzler [2c]	1943	34	Normal	Normal	Normal	Normal			168
35	Larkin, DeSanctis and Margulis [1]	1944	2	4 3	6 900	5% Eosinophils	11 Gm			275
36	Spain and Toby [27]	1944	51	3 5	8 500	Polymorphonuclear cells	8 5 Gm			
37	Baumgartner [28]	1944	40		Normal	4% Eosinophils				
38	Baumgartner [28]	1945	56	4 6	5,300	5% Eosinophils	83%			
39	Friedman [2b]	1945	23	3 7	Leukopenia	Stab cells	11 Gm	Moderately cellular		188
40	Arnold [29]	1945	27		12 100	Eosinophils				180
41	Ives [10b]	1945	53	Normal	1,000	Normal				
42	Ungar [2d]	1946	37	Anemia	18,000					
43	Zee [30]	1946	23		3,200					
44	Bendel	1946	35	4 2	7,400	Normal	13 4 Gm			183

of tissue, measuring 2 by 0 6 cm , composed of a moderate amount of finely lobular grayish white fat Serial sections revealed a pale, dull, homogeneous, grayish white surface The tissue submitted was firm, nonfriable, definitely rubbery, lobular and grayish white

"*Microscopic Examination*—1 Sections revealed chronic cystic mastitis, no malignant changes

"2 Sections consisted of a cutaneous biopsy specimen, partially covered on one side by squamous epithelium showing no evidence of epithelial changes, and a small subcutaneous nodule The upper portion of the cutis was essentially normal A slight lymphocytic infiltration in the perivascular space was noted in the lower portion of the cutis The chief pathologic changes were noted in the subcutis and adjoining fat in the form of a proliferative atrophy of the fatty

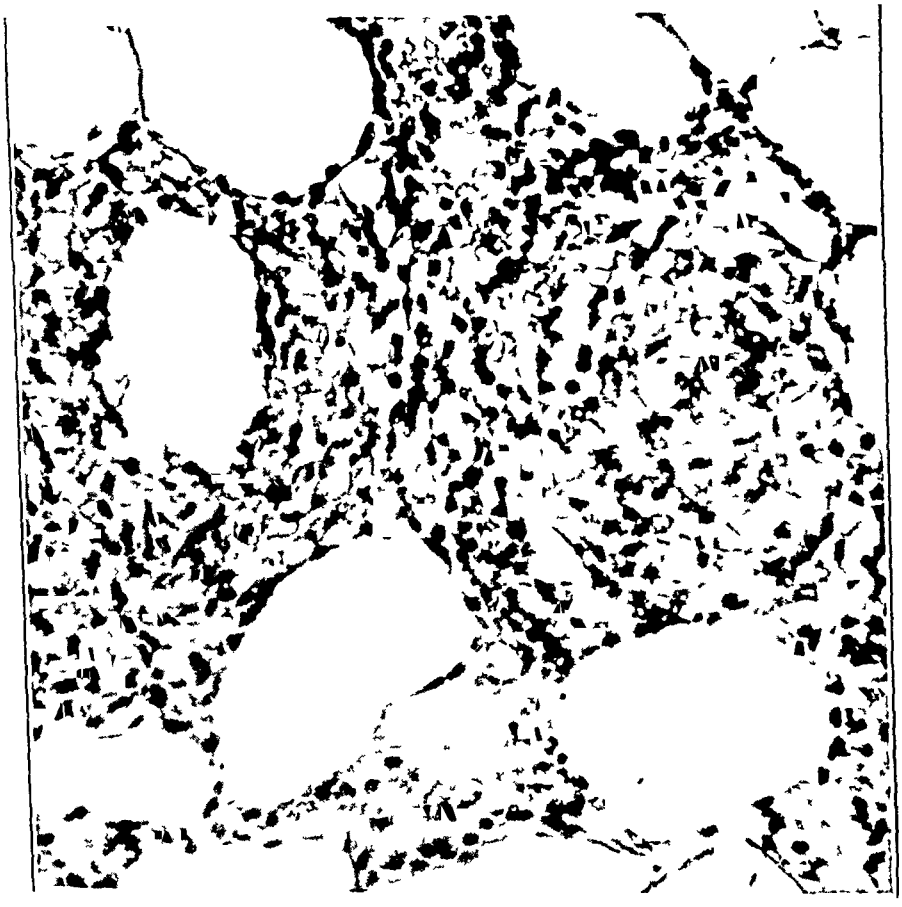


Fig 4—Rather dense inflammatory infiltration by lymphocytes, monocytes and plasma cells

tissue The latter contained numerous solitary and coalescing tubercle-like lesions composed of slightly acidophilic, epithelioid-like lesions arranged in a concentric or diffuse manner (fig 1) A few large foam cells were noted in some areas (fig 2) A sprinkling of small lymphocytes could be found in some of the sections Numerous giant cells, some being typical Langhans cells, were noted (fig 1) An occasional Touton cell could be identified Apparently some of the lesions were centered around small capillaries, but there was no evidence of intimal proliferation or medial thickening No evidence of caseation was seen Between and within these lesions, numerous small oval or round clear spaces corresponded to the remains of subcutaneous fat which had not been infiltrated (fig 3)"

TABLE 2.—*Review of the Laboratory Data on Forty-Four Cases o*

Case No (Continued)	Blood Agglutination Tests									Smear, Culture, Inoculation of Material from Lesions	Liver Function Tests
	Weltmann Coagulation Band	Br Melitensis	Paratyphoid Bacillus	E Typhosa	Typhus Organism	Past Tularensis	Str Hemolyticus A	Tuberculin Test	Blood Serology		
									+	—	
								—			
								1+			
		—							—	—	
		—							—	—	
		—						4+ 2d test			
									+		
		—	—	—					—	—	
		—	—	—		—		—	—	— for tuberculosis, lepra	—
									—		
									—		
								—	—		
		—				—			—	—	
								—		—	
								+	—	—	
								+		Staph aureus — for tuberculosis	
		—	—	—	—				—		
								—		—	
				—	—				—	— for lepra on skin	
								—		— for lepra on skin	
									—		
								—	—	—	
								—	—		
									—	—	
								?	—		
								—	—	—	
									—		
									—		
		—					—	—	—	—	3+ Cephalin flocculation
								—	—	—	
		—	—	—					—		2+ Cephalin flocculation
										—	
									—		
		—	—	—				—		—	
	Left to 0							—	—		
								—	+	—	
		—	—	—							
								—	—		

from glomerulonephritis shortly after acquiring panniculitis, and nodules of fat necrosis were found in the pretracheal, omental and mesenteric fat as well as in the panniculus adiposus In Friedman's case a staphylococcic septicopyemia was the true cause of death, although the death was attributed to panniculitis In Ungar's case the patients died from streptococcic peritonitis hematogenously spread from the tonsils It is interesting to speculate that possibly the tonsils were the source also of the panniculitis, and this would further reinforce the idea that Weber-Christian disease is not the cause but rather the effect of some distant infection This theory will be discussed further when the etiology is considered In the other 38 cases in the literature, the course seems to have been one of chronicity with frequent relapses In the few cases in which the disease appeared to have been permanently arrested the patients were not observed long enough to warrant the conclusion, a possible exception was Gilchrist and Ketron's case, which was reported without a recurrence as late as 1943,[2c] having been first reported in 1916

A review of the laboratory data collected on the 44 cases reveals nothing significant (see table 2) A leukocyte count below 5,000 was noted in 8 cases, one above 15,000 in 3, moderate leukocytosis in 4 and a normal leukocyte count in others A red blood cell count below 4,000,000 was found in 8 cases, none of a severe form of the disease Moderate eosinophilia and relative lymphocytosis were noted in a few cases Sternal marrow was normal in 3 cases, as were total blood lipids in 2 cases The blood cholesterol was moderately elevated in 1 case[1] and considerably elevated in 1 other[26] In the 14 others reported there was no deviation from normal, an important point to be considered later in discussion of the etiology The amount of cholesterol ester was normal, with the exception that it fell from normal to 10 per cent in Miller's case as death approached, this manifestation indicating hepatic damage The proportion of serum phosphatase was elevated slightly in 2 cases and was normal in 2 others Amounts of inorganic phosphorus, sugar, urea nitrogen, calcium, chlorides, bromides and uric acid in the serum were all normal The ratio of nonprotein nitrogen was elevated severely in Spain's case, in which the patient died from uremia Plasma proteins were not remarkable in variation from the normal range Cultures of the blood were negative, and cultures, smears and inoculations of material from nodules produced no organisms in 21 cases, in 1 case[15] only were blood cultures and nodule cultures positive for staphylococci, and I list this case as one of the 2 not particularly well authenticated Blood agglutination tests for Brucella melitensis, the paratyphoid bacillus, Eberthella typhosa, the typhus organism, Pasteurella tularensis and hemolytic streptococci all had negative results The erythrocyte sedimentation rate appeared to be elevated moderately in

4 cases and appreciably in 3, it closely paralleled the clinical course in 1 [29] In the last-mentioned case also the Weltmann coagulation band was found to conform to the state of the patient The Weltmann test was not used in any of the other reported cases Reactions to the tuberculin test were negative in 15 cases and positive in 4 others Reactions to serologic tests of the blood were positive in 3 cases and negative in 27 Urinalysis was normal except in 3 of the fatal cases, in which it revealed albumin (1 to 3 plus) The basal metabolic rate was slightly low in the majority of the cases in which it was taken Roentgenograms of the thorax, the long bones, the sinuses, the skull and the pelvis were normal, with the exception that cardiomegaly was revealed in 2 cases In 3 cases there was periapical dental abscess, and in 2 roentgenologic examination showed splenomegaly Laboratory procedures, such as tests for blood lipase and for fatty acids, the Frei test, gastric analysis, patch test with halogens and cutaneous tests with trichinella larvae all gave normal findings In Friedman's case there were repeatedly positive reactions to cutaneous testing with coccidioidin, and healed lesions of coccidioidomycosis were found at autopsy Review of these numerous laboratory tests reveals that they shed no light on the causation or, with the possible exception of the erythrocyte sedimentation rate and the Weltmann coagulation reaction, on the course of the disease, nor do they establish diagnostic criteria

The pathologic picture has not been specific and has varied to some degree in most of the cases described The usual gross appearance is that of small subcutaneous nodules, usually on the thighs or legs at first, which may or may not be tender, which frequently show no disturbance of the overlying skin but may exhibit ecchymosis and even occasionally ulceration and which are usually ill defined and almost fluctuant These may coalesce to form large nodules On healing, there is usually a depressed area, which is permanent and corresponds in depth to the thickness of the panniculus Microscopically, the epithelium is usually little altered The corium may show edema and increased vascularity [16] In early lesions lipolytic histiocytes (macrophages) derived from the cells of reacting tissue [6] appear in the fat spaces and produce a foam cell appearance by the ingestion of fine droplets of the fat, which appears to have been altered so that it behaves as a foreign body, calling forth a foreign body response Between the fat spaces, lymphocytic infiltration is seen As time goes on, the foam cells regress and the nuclei tend to fuse, this development giving the cells the appearance of giant cells As this activity is taking place, the stroma becomes more densely infiltrated with lymphocytes and mononuclear cells, which obliterate the empty fat spaces in many places An interesting early finding may be the swelling and thrombosis of the smaller blood vessels [19] The larger arterioles may show edema of the muscularis, with divided endothelial proliferation Around the larger

Weber-Christian Disease Reported in the Literature (Modified from Larkin, DeSanctis and Margulis[1])

Distribution of Lesions									
Face	Arms	Trunk	Legs	Other Parts	Secondary Atrophy	Local or Systemic Infections	Drugs	Remarks
−	−	−	+		+	Syphilis		
−	−	−	+		+			
−	−	−	+		−	Dental caries	Bromides	
−	−	−	+		+			
−	−	−	+		+	Tonsillectomy four years before	Quinine, salicylates	
−	−	−	+		+	Dental caries		
−	−	−	+		−	Syphilis	Iodides caused exacerbation	Pus in nodules
−	−	−	−		+	Tonsillitis, dental caries		
−	−	−	−		+	Tonsillitis, dental caries	Iodides (?)	
−	−	−	−		+	Tonsillitis, dental caries	Iodides	
−	−	−	+		+	Tonsillitis, dental caries	Bromides	
−	−	−	+		+	Tonsillitis	Bromides	
−	−	−	+		+	Tonsillitis, dental caries	Iodides caused exacerbation	
−	−	−	+		+			
−	−	−	−		+	Dental caries		
−	−	−	+	Feet	+	Dental caries		
−	−	−	+		+	Tonsillitis, dental caries (?)		Liquefaction in nodules
−	−	−	−	Breast	+	Staphylococci cultured in blood, tuberculosis (?)		Staphylococci in nodules
−	−	−	+	Breast	+	Tonsillitis, dental caries		Liquefaction in nodules
−	−	−	+	Hands, face	+	Patient convalescing from typhus		
−	−	−	+		+			
−	−	−	+		+	Tuberculosis, avitaminosis		
−	−	−	−		+	Dental caries		
−	−	−	+		+	Dental caries		Endomyocarditis
−	−	+	+	Face	+	Pleurisy, pericarditis		
−	−	−	−	Breast	?	Abortion previously (?)		
−	−	−	+		+			
−	−	−	+	Head, neck, penis	?			
−	−	−	−	Chest	+			
−	−	−	+	Shoulder	−	Possible tuberculosis		
−	−	−	+		−	Hydrocephalus		
−	−	−	+		−	Prolonged diet for gallbladder disease	Iodides, bromides precipitated lesions after syndrome established	
−	−	−	+		+	Dental caries		
−	−	−	+	Buttocks	+	Extractions of infected teeth	Sulfonamide therapy	
−	−	−	+	Feet	+			
−	−	−	+	Visceral nodules	−	Chronic glomerulonephritis		
−	−	−	+	Buttocks	−	Tonsillitis		
−	+	−	+	Buttocks	−	Tonsillitis		
−	−	−	−	Breast, buttocks	+	Extraction of infected tooth		Mitral insufficiency
−	−	−	+	Chest	?			Splenomegaly
−	−	−	−		+	Ulcer on arm from burn	Sulfapyridine therapy	
−	−	+	+	Viscera involved	−	Syphilis, streptococcic tonsillitis	Iodides caused exacerbation	Spontaneous rupture of nodules
+	−	+	−		?	Previous war wounds	Penicillin therapy	Pus in nodules
−	+	−	+		−			
−	−	−	−					Cystic mastopathy

§ Death from chronic glomerulonephritis, Weber Christian disease at death Autopsy
‡ Death from Weber Christian disease Septicemia, with Staph albus and Staph aureus Autopsy
† Death from Weber Christian disease Peritonitis, with hemolytic streptococci Autopsy

rheumatism and panniculitis, and Keil [38] attempted to classify panniculitis

The etiology of this disease is in doubt A survey of table 1 reveals that patients in 34 of the cases were female and 10 were male, a ratio of over 3 to 1 The patients in only 9 of the cases were under the age of 20, and only 3 of them were infants The syndrome appears to affect predominantly persons who are middle aged, with several patients being elderly One interesting hypothesis advanced as to etiology is that the disorder represents in adults the same disease as subcutaneous fat necrosis does in the newborn [39] In the latter condition it is generally assumed that obstetric trauma, acting on the fat with a high melting point which is present in the newborn infant, is responsible for the condition Chemical analysis of the subcutaneous fat in the newborn child reveals that only 65 per cent of it is in the form of oleic acid, as contrasted with 86 per cent of this substance in adult fat, the difference is made up by fats, such as palmitic acid,[40] with higher melting points Although it does not seem feasible to assume that the Weber-Christian syndrome is merely an adult form of adiponecrosis subcutanea neonatorum, it is interesting to note that to date no chemical analysis of the subcutaneous fat has been reported in the Weber-Christian syndrome It may be noted that infants with subcutaneous fat necrosis of the newborn are usually systemically healthy with no fever, that the disease is not thought to occur after the age of 6 months, when the chemical character of the fat in the infant becomes adult, and that the blood lipids and all the fractions are definitely increased, the iodine number being decreased [41] in this disease, reversion to normal values occurring on recovery, in addition, there are usually no residual depressed areas at the sites of the lesions

The clinical picture strikes one as an unusually active type of lipolytic response in the subcutaneous, and possibly, in some cases, visceral, fatty tissues to some hematogenously disseminated noxa Extensive tuberculin tests carried out by Shaffer with types of tuberculin derived from various sources demonstrated only the grade of allergic response present in most adults in the patient's locality, certainly in Shaffer's case it can be said that anergy did exist, so that a sarcoid-like reaction could be ruled out Furthermore, in tuberculin tests car-

38 Keil, H Panniculitis Its Place in Nosology, Brit J Dermat **47** 512-521 (Dec) 1935

39 Moore, R A A Textbook of Pathology, Philadelphia, W B Saunders Company, 1944, pp 694-695

40 McIntosh, J F , Waugh, T R , and Ross, S G Sclerema Neonatorum (Subcutaneous Fat Necrosis), Am J Dis Child **55** 112-123 (Jan) 1938

41 Luzzatti, L , and Hansen, A E Study of the Serum Lipids in Sclerema Neonatorum, Proc Soc Exper Biol & Med **46** 325-329 (Feb) 1941

of the Weber-Christian Syndrome Reported in the Literature

Blood																
Cholesterol Ester, Mg / 100 Cc	Iodine Number	Serum Phosphatase, Mg / 100 Cc	Serum Inorganic Phosphorus, Mg / 100 Cc	Sugar, Mg / 100 Cc	Urea Nitrogen, Mg / 100 Cc	Non-protein Nitrogen, Mg / 100 Cc	Calcium, Mg / 100 Cc	Chlorides, Mg / 100 Cc	Bromides, Mg / 100 Cc	Uric Acid, Mg / 100 Cc	Plasma Protein, Gm / 100 Cc	Albumin, Gm / 100 Cc	Globulin, Gm / 100 Cc	Culture of Blood	Erythrocyte Sedimentation Rate
														—	
														—	
														—	
			4.2	106										—	
														—	17 mm / hr
									Normal					—	
														—	
														—	
Normal	Normal	Normal	Normal			Normal	10 9 Normal	Normal	Normal						
				75 85	12									—	
122				83 8										Staph aureus	
				96										—	
				89		40								—	
														—	Normal
				87 5										—	36 mm / hr
														—	20 mm / hr
			3 2	124	9 4					4 1				—	
			4 26	76 5	13 5		10 5	490	Less than 75	2 68					
Normal to 10%	Normal	6 6 Bodansky units	Normal			Normal	10 3	500	Less than 75		Normal to 6 2	2 4	2 7	—	Normal
145					20	39 5			Normal						
		4 8 Bodansky units				272					6 1	4 1	2 0		15 mm / hr
														—	60 mm / hr
		6 7 Bodansky units	3 9	82 83	21						5 2 5 7			—	58/86
							8 3				7 3				10 mm / hr
															Parallel to clinical course
														—	
														—	
														—	21 mm / hr

(Table continued on next page)

The possibility that it may be a primary disturbance of lipid metabolism does not seem warranted in view of the almost invariably normal values for total blood lipids, cholesterol and cholesterol ester, in addition to the fact that the disease is rarely distributed over most of the body but usually affects one or a few parts alone An interesting observation was recently made by Duran-Reynals,[32b] who compared the Weber-Christian disease in human beings with an epidemic of a fat-necrotizing disease in rabbits in 1932 to 1934 and found the diseases to be quite similar This investigation would tend to support the theory of an infectious nature of the syndrome without, I believe, ruling out the role of allergy from the infectious agent or agents, nor would it remove the part played by halogens, the hypothesis embracing the idea that the allergy is nonspecific, resulting in Duran-Reynals' cases from some particular organism, as it apparently did in the cases in which tonsillitis or dental caries would appear to have been a predisposing factor

In making a diagnosis of the Weber-Christian syndrome, one must first distinguish between those conditions which involve the fat lobule only secondarily and those in which the adipose tissue is primarily affected Certain diseases may simulate the Weber-Christian syndrome clinically but be entirely different pathologically

Nonspecific inflammatory lesions, such as cellulitis, may extend into adjacent fat, but such a picture is rarely misinterpreted Although erythema nodosum and erythema induratum may be characterized by exudative and granulomatous inflammation of the subcutaneous adipose tissue, the fibrous septums separating the fat lobules and the connective tissue of the dermis are involved as severely as is the fat Clearly defined angiitis is commonly seen in the various types of erythema but is not prominent in panniculitis In cases of the true Weber-Christian syndrome, one is struck by the localization of the exudative and proliferative reaction to the fat lobule itself The interlobular fibrous septums may be thickened, but they are relatively spared It can be seen that the involvement of the dermis which does exist is due to inflammation of the adipose tissue about the appendages and accessory structures Erythema nodosum is usually of shorter duration, with frequent seasonal recurrences, definite tenderness and bruiselike changes Giant cells are rarely seen [43] Erythema induratum usually has a protracted course, with involvement of the overlying epithelium with necrosis and ulceration It may occasionally be found only in the subcutaneous fat Usually, however, the degree of *Wucherungsatrophie,* the specific tubercle formation, the epithelioid cells, the

43 Pillsbury D M Sulzberger M B and Livingood C S Manual of Dermatology Philadelphia W B Saunders Company, 1943, p 13 and p 290

he Weber-Christian Syndrome Reported in the Literature—Continued

inal uid	Urine	Basal Metabolic Rate	Miscellaneous Tests	Roentgenograms
	—		Normal findings in gastric analysis	Slight gastroptosis, possible "slight hilar tuberculosis"
	—	— 2%		
—		—11%		Thorax normal
		— 3%		
	—			Thorax normal, two areas of periapical infection (dental)
				Thorax normal
				Normal findings except for cholelithiasis and poorly functioning gallbladder
	—			Thorax normal
	—		Negative results in Frei test	Thorax normal
			Fatty acids in blood normal	Thorax and bones normal
				Legs normal
	—	—11%	Urinalysis normal, patch tests negative for halogens	Sinuses, pelvis, sacrum, teeth, skull, thorax and spinal cord normal, moderate splenomegaly
	—			
	—	—10%		Thorax, long bones, gastrointestinal tract and skull normal, periapical abscesses (dental)
	3+ albumin			
	—			Thorax normal, periapical abscesses (dental)
	—			
	—		Blood lipase normal	Thorax and right lower extremity normal
	—			
	—	+ 3%		Nonfilling gallbladder
	—	—15%		
	1+ albumin	— 5%		Sinuses, thorax and right thigh normal
	—			Ankles and feet normal
—	2+ albumin		Melena, skin negative for trichinella	Thorax and abdomen normal
			Test of skin with coccidioidin, 4+	Heart enlarged, mitral type insufficiency
	—			Heart enlarged
				Sinuses and thorax normal
	—			Thorax, sella turcica normal, splenomegaly revealed by abdominal flat plate
	—			Thorax normal

Similar pathologic pictures with dissimilar clinical features can be produced by various agents Localized atrophy and tumefaction of subcutaneous fat have occurred in persons after injection of insulin, camphor, oil and other agents [47]

Subcutaneous fat necrosis of the newborn has already been discussed [48]

Diffuse atrophy of subcutaneous fat without evidence of previous inflammatory changes (lipodystrophy) as a rule offers no difficulty in the differential diagnosis In this condition there is complete removal of the subcutaneous fat from the affected areas [49] The face and neck are usually affected, but Bigler has reported a case in which the loss of fat was on the legs [50]

Primary involvement of the fat lobule occurs in traumatic fat necrosis, which may closely simulate the Weber-Christian syndrome Indeed, many cases previously diagnosed as traumatic fat necrosis, particularly of the breast, without the history of trauma, may possibly have been examples of the Weber-Christian syndrome of mild localized degree, and the concomitant nodules on other parts of the body, such as the legs, may have passed unnoticed Binkley [10a] stated the belief that the syndrome should be considered in any case of possible traumatic fat necrosis or carcinoma of the breast

The types of lipogranuloma described by the Russian pathologist Abrikossoff [51] should be mentioned The nodules were observed in obese persons during the period of convalescence from infectious diseases, especially relapsng fevers and typhus The lesions made their appearance predominantly in the panniculus adiposus but also in the retroperitoneal adipose tissue, the omentum and the mesentery Although the original papers were not available to me it appears from the summaries by Abrikossoff that the Russian authors were referring to a pathologic process in many respects similar to that seen in the Weber-Christian syndrome

47 (*a*) Rowe and Garrison [32f] (*b*) Sundwall, J Localized Areas of Atrophy of Fat Cells in Derma and Subcutaneous Tissue, J Cutan Dis **36** 145 (March) 1918

48 (*a*) Shong, G, and Cowan, A Subcutaneous Fat Necrosis of New-Born, Ohio State M J **31** 34-35 (Jan) 1935 (*b*) Tow, A Scleroderma (Adiponecrosis Subcutanea Neonatorum) in Diseases of the New-Born, New York, Oxford University Press, 1937, p 436

49 Parmellee, A H Lipodystrophy, in Brenneman, J Practice of Pediatrics, Hagerstown, Md, W F Prior Company, Inc, 1936, vol 1, chap 41, pp 1-7

50 Bigler, J A Loss of Subcutaneous Fat of the Lower Extremities (Lipodystrophy), J A M A **112** 627-628 (Feb 18) 1939

51 (*a*) Abrikossoff, A, cited by Friedman [2b] (*b*) Abrikossoff, A, cited by Ungar [2d]

venules definite lymphocytic infiltration is seen The changes are seen early and persist in the older lesions The last stage would appear to be fibrosis, with healing Ungar expressed disagreement with this classic description in part and said that histologically the initial lesion is distinguished by leukocytic stasis in the blood capillaries and focal suppurative inflammation in the adipose tissue These manifestations are followed by the development of granuloma-like lesions, which arise on the axis of the fibrous septums, the process terminates in scar-like formation, or foci or foamy cell alteration Shaffer [10c] stated that the last-mentioned process results in liquefaction, as demonstrated by the loss of outline of the foam cells, with development of an amorphous foamy matrix in which the vesicular nuclei as well as the inflammatory round and polymorphonuclear cells are suspended

As was stated previously, the pathologic picture is not specific, and similar pathologic changes resulting from actual trauma [31] or the injection of oily and other foreign substances, bacterial and nonbacterial [32] particularly of insulin [32f] and recently even of various physiologic solutions [33] have been seen Friedman mentioned a case of "cold allergy" in which the application of ice to the forearm gave a histologic picture indistinguishable from the Weber-Christian syndrome [34]

All the cases of the Weber-Christian syndrome have one major feature in common involvement of subcutaneous or visceral fat alone but this feature may also be found in other conditions, in which it plays a minor role, Weber and Gray [35] reported a case in which there were inflammatory changes in the muscle as well as in the subcutaneous fat and which they therefore called an instance of "polydermatomyositis" Clerici [36] and Stockman [37] discussed the relationship of chronic muscular

31 (*a*) Adair, F E, cited by Binkley [10a] (*b*) Berner, O, cited by Bailey [2a] (*c*) Binkley [10a] (*d*) Heyde, M, cited by Bailey [2a]

32 (*a*) Alderson and Way [11] (*b*) Duran-Reynals, F A Necrotizing Disease in Rabbits Affecting Fatty and Muscular Tissues Analogies with Weber-Christian Disease of Humans, Yale J Biol & Med **18** 583-594 (July) 1946 (*c*) Eeg-Olofsson, R, cited by Rowe and Garrison [32f] (*d*) Harbitz, H J, cited by Bailey [2a] (*e*) Lux, L, cited by Bailey [2a] (*f*) Rowe, A H, and Garrison, O H Lipodystrophy Atrophy and Tumefaction of Subcutaneous Tissue Due to Insulin Injections, J A M A **99**·16-18 (July 2) 1932

33 (*a*) Netherton [12] (*b*) Schwarzmann, J M, cited by Bailey [2a]

34 Keil, G J, and Fromer, J, cited by Friedman [2b]

35 Weber, F P, and Gray, A M H Chronic Relapsing Polydermatomyositis with Predominant Involvement of the Subcutaneous Fat (Panniculitis), Brit J Dermat **36** 541 560 (Dec) 1924

36 Clerici, A Chronic Muscular Rheumatism and Panniculitis, Gazz d osp **49** 585-587 (May 13) 1928

37 (*a*) Stockman, R British Medical Association Lectures on Chronic Muscular Rheumatism and Panniculitis, Brit M J **1** 293-295 (Feb) 1928, (*b*) Causation of Fibrositis and Panniculitis, M J & Rec **128** 466-467 (Nov 7) 1928

suggested that the mechanism may be in the form of a nonspecific type of allergy The liquefaction and pus occasionally occurring in the nodules probably indicate merely a severer phase of the more commonly seen nonsuppurative reaction A somewhat different view was propounded by Ungar,[2d] who stated the belief that nonsuppurative changes are due to tissue injury by fatty substances liberated in the course of destruction of fat cells by suppurative inflammation In either instance, however, it would appear that the nonsuppurative changes have no specific significance in the pathologic process of the Weber-Christian syndrome

SUMMARY

1 The syndrome relapsing febrile nodular panniculitis, or Weber-Christian disease, is discussed and the forty-fourth case reported

2 The literature is reviewed, and the pertinent points are summarized in two tables

3 The pathology and etiology are discussed, and the suggestion is advanced that the etiology may be on the basis of a nonspecific tissue allergy

4 The differential diagnosis and treatment are presented

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ried out on many of the other patients, some reactions were positive (which finding would rule against sarcoid) and others were negative (which observation is a point against tuberculosis) In Shaffer's case a Berkefeld filtrate of the aspirated contents of an early lesion failed to produce a reaction when injected intracutaneously or subcutaneously Furthermore, a careful study of the sections failed to show any of the more or less characteristic features often seen in virus disease, such as balloon degeneration and inclusion bodies [10c] It appears obvious that bacteria per se are not the cause, as is shown by the almost universally negative results in cultures of blood and in smears, cultures and inoculations of the nodular material The 1 case, Puente's, in which staphylococci were found, as has already been mentioned, must be regarded with suspicion Arnold [29] noted that dermatitis herpetiformis, as did his case of panniculitis, also responds to sulfapyridine more regularly than to any of the other sulfonamide compounds and that it appears to be caused by bacterial allergy It is certainly difficult to by-pass the fact that in 10 of the 11 cases there was a fairly sound history either of development of the syndrome after the receiving of the halogens iodine and bromine or of exacerbation of the syndrome by the halogens after its establishment. In Rosenberg and Cohen's 2 cases and in Weber's second case, the onset of a relapse with appearance of fresh nodules and a spike in temperature could be produced at will by administration of a halogen and the reaction as promptly disappeared on discontinuance of the medication The role of local or systemic foci of infection appears prominent when one consults table 1 Almost every patient had some infection or possible predisposing factor in this column, and 21 gave a picture of either dental caries or tonsillitis or both In some instances the role of prolonged diet of one sort or another was emphasized [42] There appears to be a gradual progressive change in the fat of the subcutaneous tissue of the skin, and possibly of the visceral fat in the severer cases, due to some unknown cause I would suggest that the cause is an allergy of some sort, either bacterial or chemical, possibly even of virus origin, which produces the metamorphosis in the fat This metamorphosed fat then acts as a foreign body in the tissues and calls forth a foreign body inflammatory reaction, such as is seen in pathologic study of the disease This opinion, of course, is based only on a statistical survey and as yet is not substantiated by known fact One is impressed with the very limited investigative work previously carried out on the panniculus adiposus, and also one is interested to note that the structure possesses definite physiologic functions and properties and that it can have certain pathologic variations

42 (*a*) Rosenberg and Cohen [26] (*b*) Tilden, Gotshalk and Avakian [19]

it to be the most satisfactory method yet devised for the treatment of psoriasis, which, however, it did not cure

I felt that a certain technic was necessary if photodynamic action were to be achieved by the procedure and that this action could be enhanced by further modification of the solutions of crude coal tar employed This paper presents the results of the studies of these problems

METHODS AND RESULTS

The current method of attempting to produce a photodynamic response in the skin with tar consists in painting an area with solution of coal tar N F (a 20 per cent solution of coal tar in alcohol, with quillaja) and irradiating the area with a mercury vapor arc lamp as soon as the applied solution has dried The following experiment shows that this procedure does not produce any photochemical reaction on the treated skin

Solution of coal tar N F and 5 per cent solutions of crude coal tar in acetone, alcohol, carbon tetrachloride, chloroform and ether, respectively, were each painted on corresponding sites on both forearms and the dorsa of 6 subjects The solutions were permitted to dry, and immediately afterward the right side was exposed to an erythema dose of ultraviolet radiation from a mercury vapor lamp, while the left side was covered Following this treatment, the left side was exposed to an erythema dose of ultraviolet radiation from a carbon arc lamp using a sunshine® carbon electrode, with the right side covered Then the same solutions were applied on fresh sites, on the forearms and the dorsa of 6 subjects In this second experiment the applications were made daily for three consecutive days, and immediately after the last application the subjects were exposed to erythema doses of light from both the mercury vapor and the carbon arc lamps, as on the earlier occasion

In each case the areas to which the various tar solutions had been applied showed no effect from the exposure to light, whereas the surrounding zones displayed a bright erythematous reaction

The failure of the tar solutions to produce photosensitization in this instance was due to the fact that the surface film of tar acted as a screen or filter which prevented the radiation of specific wavelength from reaching the skin

To demonstrate that crude coal tar solutions can produce photosensitization, the following experiments were done

The six solutions used in the former experiment were applied to the sides of both forearms and the dorsa of 6 subjects for three consecutive days On the fourth day the areas were washed thoroughly with soap and water and afterward with alcohol This washing removed only the surface film of tar, as under the Wood light the areas which had been painted and then washed still fluoresced brightly The right side was then exposed to an erythema dose of ultraviolet radiation from a mercury vapor lamp, with the left side covered, and, next, the left side was exposed to an erythema dose of light from a carbon arc lamp using a sunshine® carbon, with the right side covered

"rosette giant cells" and the pronounced vascular changes distinguish it histologically

The subcutaneous sarcoid of Darier and Roussy may offer clinical similarities, but this condition does not usually lead to the loss of subcutaneous fat and the resultant depression on involution of the lesion, and it shows histologically such characteristics as epithelioid tubercles, pronounced fibroblastic proliferation, periarteritis and periphlebitis which help to distinguish it from the Weber-Christian type of panniculitis The variation in reactions, depending on the degree of anergy present precludes too much dependence on the tuberculin test in a differential capacity Goeckerman [44] called attention to the fact that it may be impossible to differentiate sarcoid and erythema induratum from other inflammatory processes in the early stages

Dermatomyositis involves muscle as well as skin and there is severe pain on movement and considerable muscular weakness

Nodular syphilis and leprosy can be ruled out by serologic tests and biopsy smear Dermal manifestations of the types of lymphoblastoma [45] can be diagnosed by biopsy and by attention to the systemic aspects of the disease

In adiposis dolorosa the nodules remain unchanged for years and are painful The nodules are encapsulated and composed of large numbers of small, oval fatty bodies connected with each other and with the capsule by delicate fibrous bands The capsule is composed of several layers of well developed connective tissue This tissue is highly vascular and between the vessels is a reticular tissue, denser in some areas than in others and enclosing a large number of mononuclear cells, a few polymorphonuclear cells and a large number of cells staining a tawny color by the Van Gieson method Scattered through the granular tawny masses many of the mononuclear type of cells occur In other areas granules of blood pigment are present

Rare types of thrombophlebitis [46] may show the clinical picture of relapsing febrile nodular panniculitis, but evidence of venous inflammation and thrombus formation is found in the histologic examination

Agglutination tests may be used to clarify suspicion of brucellosis, typhoid or paratyphoid that may be aroused by the relapsing type of fever associated with Weber-Christian disease

The lesions of morphea (circumscribed scleroderma) are plaque-like slow to develop and regress and leave the skin shriveled and bound to the underlying tissues

[44] Goeckerman W H Sarcoids and Related Lesions A Report of Seventeen Cases Review of the Recent Literature, Arch Dermat & Syph **18**:237-262 (Aug) 1928

[45] Reimann H A Havens, W P and Herbert, P A , cited by Friedman [2b]

[46] Barker N W , cited by Bailey [2a]

reaction with the mercury vapor lamp or the carbon arc lamp using a therapeutic C carbon electrode The work presented in this paper does not necessarily conflict with the results of Foerster and Schwartz for the reason that the carbon arc radiation was not produced in identical fashion in both series of experiments The quality of radiation from the carbon arc depends on the following factors [8] the size and the kind of electrodes, the direction of the current, when direct current is used through combinations of neutral-cored and impregnated carbons, and the amount of the electric current The limits of the effective spectrum for photodynamic action allow only the use of the sun and of the carbon arc for the production of photosensitization of the skin with tars To increase the intensity of photodynamic action on the skin beyond that reported in this paper, it will be necessary for one to take into account the factors affecting carbon arc radiation, the nature of the photosensitizing chemical and the solvent as well as the wetting agent employed in conjunction with this chemical

SUMMARY

The inclusion of a wetting agent in solutions of crude coal tar, in conjunction with the use of the carbon arc as a source of radiation, enhances the photodynamic action of such solutions on the skin

8 Coblentz, W W Sources of Ultraviolet and Infra-Red Radiation Used in Therapy Physical Characteristics, J A M A **132** 378 (Oct 19) 1946

Treatment of the syndrome has been to a large extent unsatisfactory The condition has been regarded as chronic, relapsing and self limited, with a tendency eventually to burn itself out Such an attitude should be regarded with suspicion, as it has already been shown that neither is the disease as innocuous as has been assumed, nor does it disappear so readily In the past, removal of foci of infection, discontinuance of the use of halogens, a diet high in vitamins, roentgen therapy, ultraviolet irradiation and sulfonamide therapy have all been tried, with varying success Successful treatment of 1 case was reported by Arnold who used sulfapyridine Recently, Zee obtained an apparent cure with the use of penicillin It would appear, at present, that general systemic measures, local massage and heat and a trial of the sulfonamide drugs, in adequate dosage, or penicillin give the best outlook in the treatment Miller and Kritzler [2c] expressed the opinion that the sulfonamide compounds were useless in the treatment, but from a careful analysis of their article it would appear that, the sulfonamides at the time of their writing having been in the early days of clinical trial, these authors used inadequate doses and obtained insufficient blood levels to secure the maximum therapeutic efficacy with all the three drugs (sulfanilamide, sulfathiazole and sulfadiazine) which they employed, with the possible exception of sulfathiazole [52] It may also be noted that their patient showed early satisfactory temporary improvement with small doses of sulfanilamide, treatment with which was then discontinued, possibly because of the general improvement There was an immediate exacerbation of symptoms, but afterward the patient was refractory to all of the sulfonamide drugs given

COMMENT

Although the etiology is unknown, the clinical-pathologic features suggest that panniculitis of the Weber-Christian type is a syndrome rather than a disease entity It would appear that it is the result of some noxious stimulus producing a metamorphosis in the subcutaneous fat, and possibly also in the visceral fat in the severer cases, the fat acting as a foreign body and calling forth a foreign body response, with the reticuloendothelial system playing a large part in the syndrome It is

52 (*a*) Goodman, L, and Gilman, A The Pharmocological Basis of Therapeutics, New York, The Macmillan Company, 1941, pp 1021-1103 (*b*) Useful Drugs, Council on Pharmacy and Chemistry, American Medical Association, edited by K A Hatcher, ed 12, Chicago, American Medical Association, 1941, p 205 (*c*) Kolmer, J A, and Tuft, L Clinical Immunology, Biotherapy, and Chemotherapy in the Diagnosis, Prevention, and Therapy of Disease, Philadelphia, W B Saunders Company, 1941, pp 297-298 (*d*) The Merck Manual of Therapeutics and Materia Medica, ed 7, Rahway, N J, Merck & Co, Inc, 1944, pp 986 and 1336 (*e*) Warkentin, J, and Lange, J Physician's Handbook, ed 2, Chicago, Medical Publishers, 1942, p 239

Supernumerary appendages have also been called nevus cartilaginous [7] because they most frequently contain cartilage This cartilage is a necessary part of the condition, as it proves derivation from the branchial apparatus There are three usual locations for accessory auricular appendages (1) on the tragus or in its proximate vicinity, (2) along a line drawn from the tragus to the angle of the mouth, and (3) on the sides of the neck along the sternocleidomastoid muscle

Supernumerary appendages are most commonly found on the tragus or in its immediate vicinity In the other two locations, they may be seen, though rarely

The external ear consists of the auricle, or pinna, and the external acoustic meatus Histologically the auricle consists of a thin plate of yellow elastic cartilage covered by skin anteriorly and by skin and some subcutaneous tissue posteriorly The ear develops about the first branchial cleft Three tubercles develop above the mandibular arch to form the tragus, the crus of the helix and the helix, three form from the hyoid arch to form the antihelix, the lobule and the antitragus Undoubtedly in many cases the auricular appendages are anomalies of these tubercles rather than of the branchial arch itself

Cervical auricles originate from the other branchial clefts, sometimes in association with branchial fistulas They are seen along the anterior border of the sternocleidomastoid muscle at the level of the hyoid cartilage or just above the sternoclavicular articulation

The lesions may assume many different shapes and forms Some are elevated tabs or nodules, some are small, dimple-like lesions with central teats Not in all lesions can the underlying cartilaginous plaque be palpated It is also observed that frequently these anomalies are associated with other congenital malformations It is further observed that such anomalies may appear in more than one generation of the same family—in case 2 reported here, supernumerary ears had appeared in three generations of one family

The common error made in diagnosing these cases clinically is considering the lesions to be fibromas Histologic examination of the lesion will show its true nature, since cartilage is always found high in the subcutis or in the cutis The presence of cartilage is an outstanding feature of the condition, because cartilage normally is not seen in this location The accompanying figures illustrate the presence and location of cartilage

7 Aoki in Jadassohn, J., and Zieler, K Ikonographia dermatologica Berlin Urban & Schwarzenberg, 1937 no 41 p 256

ENHANCING PHOTODYNAMIC EFFECT OF SOLUTIONS OF CRUDE COAL TAR ON THE SKIN

LAWRENCE FRANK, M D
BROOKLYN

THE WORK reported in this paper is part of a problem concerned with the development of a method for the effective treatment of psoriasis by photodynamic action

Lewin [1] was the first to recognize that coal tar products are capable of rendering the skin sensitive to sunlight He found that most of a large group of persons who came repeatedly into contact with certain coal tar products had dermatitis and itching when they were exposed to sunlight Other investigators in this field included Herxheimer and Nathan,[2] Fleishhauer,[3] Doniach and Mottram [4] and Foerster and Schwartz [5] These early workers established the fact that the action spectrum for tar lies between 3,300 and 5,000 angstrom units and that it is not possible to credit the photosensitizing action of coal tar residues very definitely to any one group of compounds [6] An attempt to employ photodynamic action therapeutically in dermatology was made by Goeckerman [7] when he applied 5 per cent crude coal tar in an ointment of zinc oxide and petrolatum to lesions of psoriasis and irradiated the area with a mercury vapor lamp He and also subsequent workers employed this procedure, unmodified and modified, and believed

From the Long Island College Hospital and the Department of Dermatology and Syphilology, Long Island College of Medicine

1 Lewin, L Ueber photodynamische Wirkungen von Ihaltsstoffen des Steinkohlenteerpechs am Menschen, Munchen med Wchnschr **60**·1529, 1913

2 Herxheimer, K, and Nathan, E Ueber Sensibilisierung der Haut durch Carboneol gegenuber Sonnenlicht und eine dadurch bedingte Dermatitis solaris, Dermat Ztschr **24**·385, 1917

3 Fleischhauer, L Ueber die sensibilisierende Wirkung des Teerpraparates Liantral, Strahlentherapie **36** 144, 1930

4 Doniach, I, and Mottram, J C Sensitization of the Skin of Mice to Light by Carcinogenic Agents, Nature, London **140** 588, 1937

5 Foerster, H R, and Schwartz, L Industrial Dermatitis and Melanosis Due to Photosensitization, Arch Dermat & Syph **39** 55 (Jan) 1939

6 Blum, H F Photodynamic Action and Diseases Caused by Light, American Chemical Society Monograph Series, no 85, New York, Reinhold Publishing Corporation 1941, p 265

7 Goeckerman, W H Treatment of Psoriasis Northwest Med **24** 229, 1925

REPORT OF CASES

CASE 1.—S. J., an 8 month old female infant, was first seen on March 4, 1942. The mother stated that she noticed a defect in the middle of the baby's right cheek at the time of birth. This defect had not changed in size, shape or color during the eight months.

Examination revealed a circular, chamois-hued, macular patch about 1 cm. in diameter just midway between the angle of the mouth and the tragus. Palpation showed it to be of the same consistency as the normal skin.

A clinical diagnosis of nevus—possibly a soft fibroma—was made. Surgical removal was advised. On April 25 the entire lesion was removed with the use of procaine hydrochloride (novocaine hydrochloride®) anesthesia and submitted as a biopsy specimen.

The histologic study (see fig. 1) was made by Dr. David Satenstein and Dr. Wilbur Sachs. The microscopic report was "development of cartilage tissue." The description was as follows: "Within the subcutaneous tissue was a large,

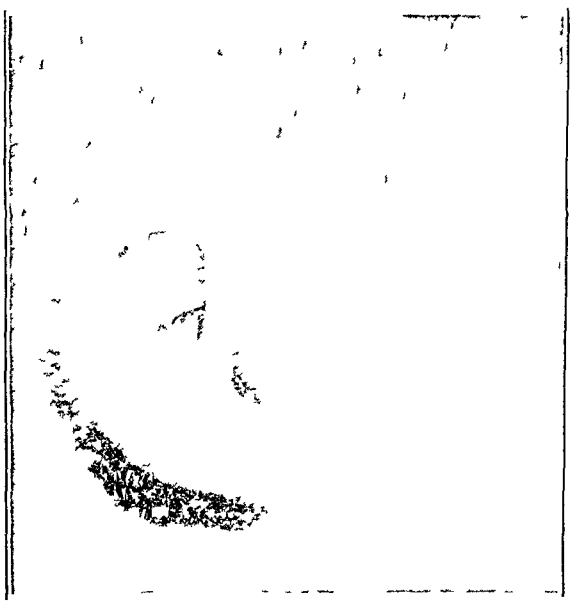


Fig. 2 (case 2).—G. K., aged 21 months, showing a chamois-colored patch 1 cm. in diameter, with a central elevation, on the right cheek. The patch had been present since birth.

oval mass of cartilage, which was surrounded by a fibrous capsule. Besides this observation (cartilage where one would not expect to find it) the slide showed nothing abnormal."

When we discussed the slide with Dr. Satenstein he suggested the possibility that the lesion was a supernumerary ear.

CASE 2.—G. K. (fig. 2) a male baby aged 21 months was first seen by us on Sept. 14, 1944. The mother stated that the baby had been born with a small mass on the right cheek and that he persistently picked and irritated it. Examination revealed a chamois-hued patch about 1 cm. in diameter, with a central elevation. Palpation showed it to be of the same consistency as the normal skin. The diagnosis of supernumerary ear was made. The mother then stated that

The results with the mercury vapor lamp were as follows Erythema of equal intensity appeared on both the painted and the unpainted areas but was more rapid in its development in the former The only materials which produced a well demarcated reaction on the painted skin, in 2 of the 6 subjects studied, were solution of coal tar N F and the solution in carbon tetrachloride With the carbon arc lamp the photodynamic reaction was greater in intensity than with the mercury vapor arc lamp and was provoked by all the tar solutions except the alcoholic The most effective solvents for the tar, as was manifested by the intensity of reaction following irradiation with the carbon arc lamp, were, first, carbon tetrachloride and, second, acetone

Having established the fact that tar solutions can be used to produce photosensitization, I then made an attempt to produce a solution which would be a more effective photosensitizer than any previously used The properties desired for this solution were, first, the ability to penetrate the skin and thus, probably, to come into more intimate contact with the reacting tissue and, second, capability of ready removal from the surface of the skin by washing It was felt that the addition of a wetting agent would accomplish both of these conditions

To demonstrate a more effective tar solution for photosensitization I performed the following experiment, in which carbon tetrachloride was selected as the solvent for the tar on the basis of the foregoing work

Five grams of crude coal tar was added to 60 cc of carbon tetrachloride, 30 cc of acetone, 5 5 cc of propylene glycol and 4 5 Gm of aerosol O T® (the dioctyl ester of sodium sulfosuccinate in 99 to 100 per cent concentration) The mixture was then filtered The filtrate, as well as solution of coal tar N F and a 5 per cent solution of crude coal tar in carbon tetrachloride, was painted on the abdomen of 6 subjects on three successive days On the fourth day the areas were washed thoroughly with soap and water followed by alcohol and were then exposed to an erythema dose of light from a carbon arc lamp using a sunshine® carbon

All three areas to which the tar had been applied showed an erythema which appeared earlier than did that on the surrounding untreated skin Twelve hours after irradiation the erythema of the painted sites was more intense than was that of the surrounding skin, and, after the third day, pigmentation was present in all three sites The coal tar solution containing the wetting agent produced the most intense reaction Next in intensity was the reaction caused by the solution in carbon tetrachloride, and least was that from the solution of coal tar N F

COMMENTS

Foerster and Schwartz [5] demonstrated the photosensitizing effects of pitch, containing a high percentage of crude coal tar, when sunlight was the source of radiant energy They were unable to obtain any

she had had similar lesions on both sides of her head (fig 3) and that they had been treated by "tying off" when she had been a child Examination of the mother showed somewhat elevated scars in front of both tragi Questioning further revealed that the maternal grandmother (fig 4) had borne a similar lesion on the right side of her head since birth



Fig 5—Cartilaginous tissue with a fibrous capsule high up in subcutis (G K, case 2)

The entire lesion was removed from the child with the use of procaine hydrochloride anesthesia and submitted for biopsy The microscopic diagnosis by Dr Wilbur Sachs was "supernumerary ear" (fig 5) The histologic description was as follows

SUPERNUMERARY EARS

Report of Three Cases

CHARLES S MILLER, M D
AND
KATE F MILLER, M D
CORONA, N Y

ANOMALIES of the branchial clefts and arches are among the commoner congenital aberrations Greater interest in these cases manifested itself in the last half of the nineteenth century, at which time many reports were added to the literature In England, Birkett,[1] Bland Sutton[2] and others[3] and in Germany, Ferdinand Schmitz[4] and Virchow[5] added materially to the subject with illustrative case reports and studies Observers in other countries have from time to time enriched the knowledge of this subject by studying and reporting cases which have come to their attention One of the most comprehensive reports was contributed by Carp and Stout[6] in 1928 These authors classified a series of 32 cases according to embryologic development

There has been a difference of opinion as to the nomenclature used By supernumerary appendages we mean the lesions occurring on the face and neck Those occurring on the face are called supernumerary auricles (or ears), and those on the neck, cervical auricles

Polyotia is a term frequently applied to the supernumerary auricles about the auditory meatus or in its proximate vicinity It is interpreted to mean more than one ear on either or both sides of the head This use is technically incorrect because the complete ear apparatus is never duplicated

1 Birkett, J Congenital Supernumerary and Imperfectly Developed Auricles on the Sides of the Neck, Tr Path Soc London **9** 448, 1857-1858

2 Sutton, J B Supernumerary Auricles, Illust M News **1**·320, 1888

3 Clarke, W B Supernumerary Auricles, Illust M News **1**.321, 1888 Lake, R Double Supernumerary Auricle, ibid **1** 322, 1888

4 Schmitz, F Ueber Fistula auris congenita und andere Missbildungen des Ohres, Halle, Lipke, 1873

5 Virchow, A Ein neuer Fall von Halskiemenfistel, Arch f path Anat **32** 518, 1865

6 Carp L, and Stout, A P Branchial Anomalies and Neoplasms, Ann Surg **87** 186, 1928

SUMMARY

Two cases of supernumerary ears along a line drawn from the anterior tragus to the angle of the mouth are reported In the first, diagnosis was made only after the histologic examination revealed the features of a supernumerary ear The second, also a case of a flat lesion but one with a central elevation, was diagnosed clinically Diagnosis was verified on histologic examination

In the third case there was a cervical auricle, and the diagnosis was made clinically

37-38 One Hundred and Fourth Street

Costello and Shepard [8] in 1939 reported on the literature and added reports of 4 additional cases Three photographs were shown in which the lesions were on the tragus or in the cheek near the tragus We wish to report 3 cases 2 in which the supernumerary ears were along



Fig 1—Showing within the subcutis a large oval mass of cartilaginous tissue surrounded by a fibrous capsule

the line from the tragus to the angle of the mouth, and a third in which a cervical auricle was found near the sternoclavicular junction

8 Costello, M J, and Shepard, J Supernumerary External Ears, Arch Otolaryng **29** 695 (April) 1939

titis, stasis dermatitis and exudative chronic discoid and lichenoid dermatosis (Sulzberger and Garbe) [5]

The patient who is the subject of this report had, on clinical examination, the characteristic manifestations of lichen planus and, in addition, moderate enlargement of several lymph nodes Microscopic examination revealed the features of lichen planus and the typical picture of lipomelanotic reticulosis So far as we know, this is the first report of lipomelanotic reticulosis in association with lichen planus

REPORT OF CASE

L H, a 70 year old woman, was first seen by us in December 1946, when she complained of an itching eruption of one month's duration The dermatosis,

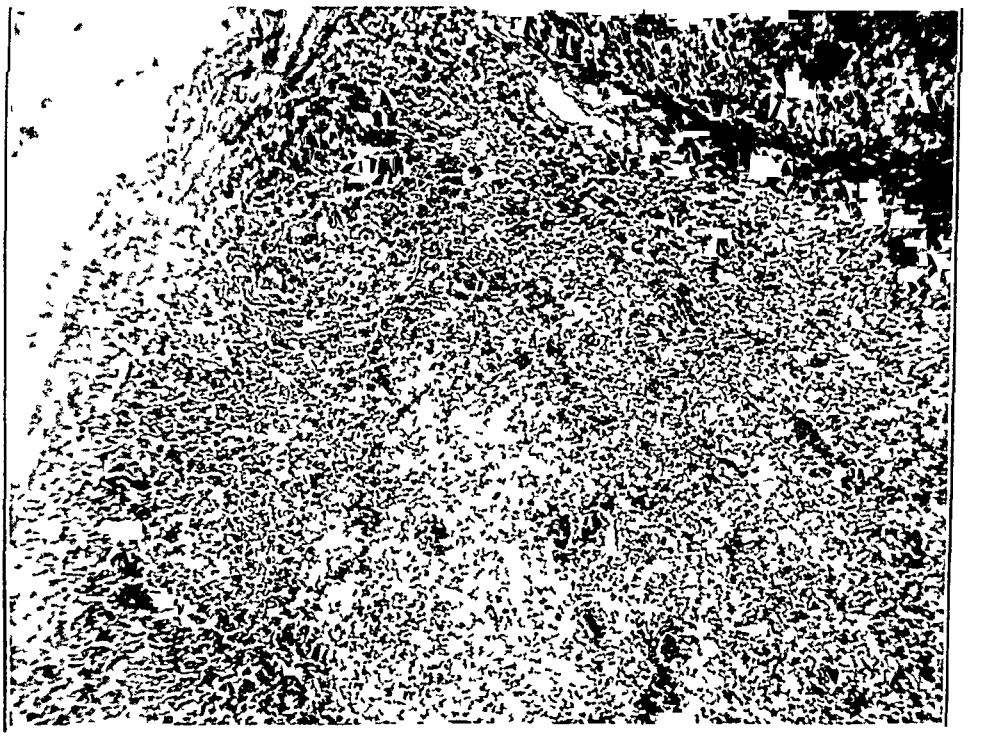


Fig 1—Granulomatous hyperplasia of lymph node in lipomelanotic reticulosis (× 22)

which had begun on her hands, spread gradually to the extremities and trunk, pruritus meanwhile increased in intensity

Physical examination disclosed features normal for a woman of the patient's age Scattered over the extremities were large and small, discrete and confluent plaques composed of the erythematous, polygonal, flat-topped papules characteristic of acute, generalized lichen planus The mucous membranes were not involved The enlarged lymph nodes in the axillas and in the groins were moderately firm but not tender Examinations of the blood, performed at intervals, disclosed no abnormalities

5 Kocsard, E Three Cases of Exudative Chronic Discoid and Lichenoid Dermatosis (Sulzberger and Garbe) (in Shanghai), J Invest Dermat **10** 1-9, 1948

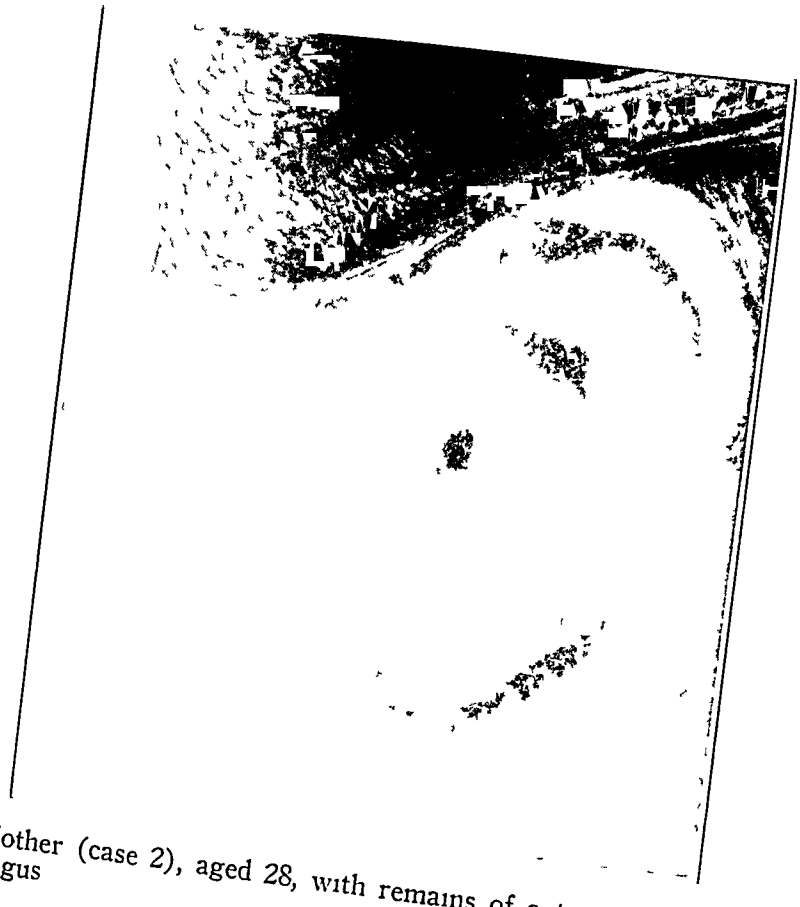


Fig 3—Mother (case 2), aged 28, with remains of a treated elevation in front of the left tragus

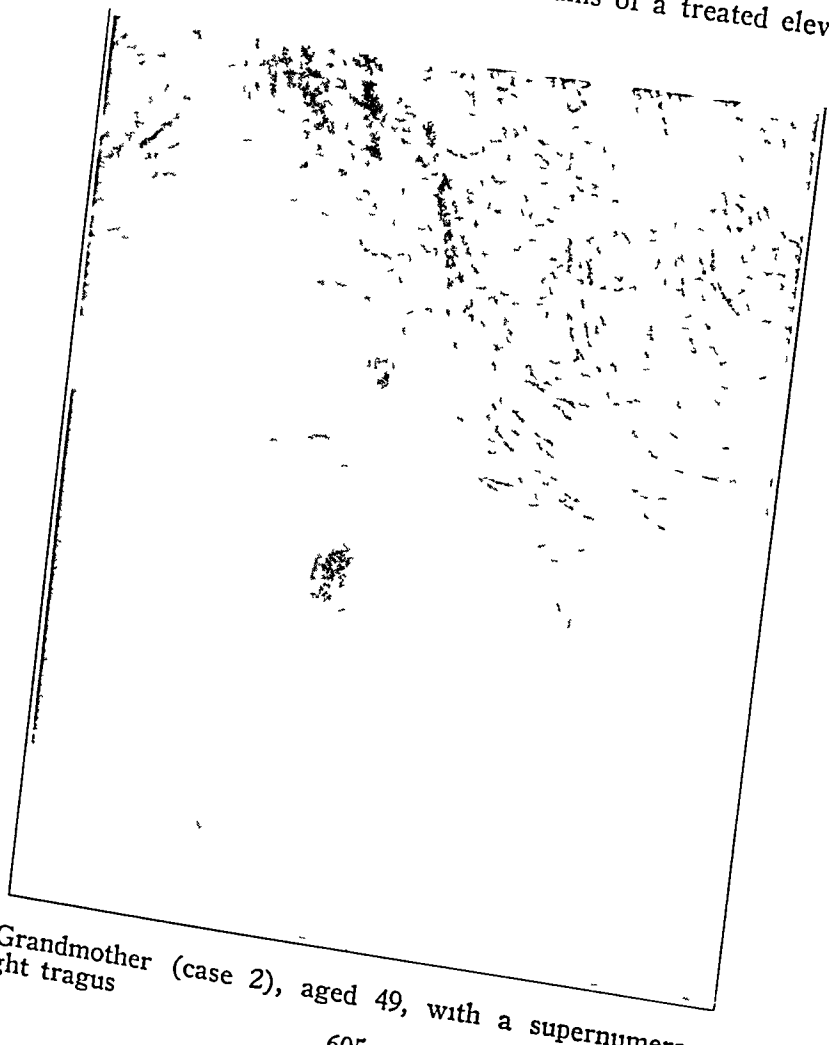


Fig 4—Grandmother (case 2), aged 49, with a supernumerary ear evident below the right tragus

Biopsy of a cutaneous specimen revealed features typical of lichen planus Microscopic study of a large node from the right groin (removed elsewhere [6]) showed that the architecture had been obscured by a proliferation of large reticuloendothelial cells, most evident in the cortex but also present in some portions of the medulla In the cytoplasm of the poorly outlined cells were vacuoles which gave a positive reaction to stains for fat Special stains indicated that the brown pigment irregularly clumped in phagocytic cells was melanin and not hemosiderin Small numbers of plasma cells, eosinophils and polymorphonuclear leukocytes were scattered throughout the excessively vascularized node

There were several severe exacerbations, but over a period of six months the eruption, as well as the enlargement of the lymph nodes, gradually subsided

COMMENT

Consideration of the features of our case and of those previously reported appears to show that in all instances the dermatoses which preceded the changes in the lymph nodes, though etiologically and morphologically widely divergent, were usually generalized, chronic or chronic-recurrent and intensely pruritic The lymphadenopathy was sometimes widespread but was usually most pronounced in the inguinal and the axillary areas Affected lymph nodes were somewhat firm, discrete and not tender Grossly, the cortex appeared clearer than normal, and the melanin stood out as scattered brown specks

The hyperplasia of reticular cells is assumed to result from their continued efforts to phagocytose large quantities of melanin and lipid material, presumably cholesterol The amount of sudanotropic material is greater [7] in nodes exhibiting lipomelanotic reticulosis than in those with most other lesions In normal lymph nodes or in those undergoing follicular or reticular hyperplasia, melanin and fat are either absent or present only in small amounts

Normally, most of the melanin formed by melanoblasts in the basal cell layer of the epidermis is eliminated in the process of keratinization, although minute amounts may be carried away by the regional lymphatics The trauma of continued scratching may result in the production of abnormal quantities of melanin, most of which pigment is transferred to the dermis Scratching may even mechanically propel pigment into dilated regional lymphatics and thence into the lymph nodes A comparable mechanism is postulated to account for the transfer of lipid material to the nodes

The amounts of lipid and melanin in the abnormal lymph nodes appear to be directly proportional to the severity and duration of the pruritus Although chronic pruritic inflammation seems to be the

6 Dr E M Butt, who removed the lymph node, placed the sections at our disposal

7 Laipply, T C Lipomelanotic Hyperplasia of Lymph Nodes Report of Six Cases, Arch Int Med **81** 19-36 (Jan) 1948

"In the center of the section, extending from the midcutis to fat, was an oval cartilaginous mass About this was a circumscribed increase in the fibrous tissue, within which there was a diffuse fibroblastic cell infiltration The vessels of the midcutis and the upper cutis were moderately dilated, and there was a considerable cellular infiltration, partly focal and partly diffuse The cells were composed chiefly of small round cells, wandering connective tissue cell and plasma cells The overlying epidermis showed no important change There were numerous hair follicles which appeared immature and not fully developed There appeared to be only a small amount of cutis present in relation to the amount of subcutis

"Diagnosis The microscopic picture was concomitant with the features found in cases of supernumerary ear Some irritation was present"



Fig 6—Cervical auricle near the left sternoclavicular articulation (case 3)

Case 3—S A (fig 6), aged 5, was seen on May 1, 1945, for herpes simplex on the right cheek Routine examination revealed a small mass near the left sternoclavicular junction Permission was not granted for its removal The clinical diagnosis was cervical auricle

COMMENT

S J, now 6 years old, has been examined at regular intervals She was last seen on Oct 10, 1945 There is a fine, soft scar at the site of the previous lesion No other sequelae have resulted from removal of the lesion

As far as we can ascertain, no tumor mass or malignant changes have developed from these supernumerary ears According to the observations by Carp and Stout,[9] in cases in which malignant neoplasms have developed they have been in association with branchial fistulas

9 Carp and Stout,[6] p 194

TREATMENT OF LUPUS VULGARIS WITH CALCIFEROL (VITAMIN D_2)

HARRY PARISER, M D
AND
JAMES W ANDERSON, M D
NORFOLK, VA

THE TREATMENT of cutaneous tuberculosis with calciferol (vitamin D_2) had its beginnings and development in Europe It is not the purpose of this paper to survey the European literature since there is an American report on this (Michelson and Steves [1]) The incidence of cutaneous tuberculosis is so much greater in Europe than in the United States that large series of cases are difficult to accumulate in this country Since the authors have had the opportunity to follow 3 cases of lupus vulgaris after treatment with calciferol it was felt that a report of their findings is justified to add to the American experience with this treatment

Calciferol is prepared by exposure of ergosterol to ultraviolet irradiation The doses of calciferol used in the treatment of cutaneous tuberculosis are large compared with the usual maintenance doses Indeed, the best therapeutic results are obtained at or near the dose which may produce toxic symptoms (Macrae [2] and Dowling and Thomas [3]) As yet the exact schedule of treatment has not been standardized A brief summary of the suggested schedules of treatment might be helpful

Feeny [4] suggested a dose of 100,000 units daily, to be raised to 150,000 units if the patient indicated tolerance or was not progressing satisfactorily He reported that this treatment was more beneficial than any other form of treatment used by him

The experience of Macrae [2] is interesting and significant He treated 20 patients in whom the infections were so far advanced that

1 Michelson, H E, and Steves, R J Treatment of Cutaneous Tuberculosis with Large Doses of Vitamin D_2, Arch Dermat & Syph **56** 317 (Sept) 1947

2 Macrae, D E The Use of Calciferol in Tuberculous Conditions, Lancet **1** 135 (Jan 25) 1947

3 Dowling, G B, and Thomas, E W P Treatment of Lupus Vulgaris with Calciferol, Brit. J Dermat. **58** 45 (March-April) 1946 Treatment of Lupus Vulgaris with Calciferol, Lancet **1** 919 (June 22) 1946

4 Feeny, P J, Sandiland, E. L, and Franklin, L M Calciferol in Tuberculosis Review of One Hundred and Fifty Cases of Lupus Vulgaris, Review of Twenty-One Cases of Pulmonary Tuberculosis, Lancet **1** 438 (April 5) 1947

LIPOMELANOTIC RETICULOSIS OF LYMPH NODES IN A CASE OF LICHEN PLANUS

MAXIMILIAN E OBERMAYER, M D
AND
ERNEST THOMAS FOX, M D
LOS ANGELES

IN 1891 Jadassohn [1] described some peculiar histopathologic changes in the lymph nodes observed in a case of pityriasis rubra (Hebra) Subsequently, Pautrier and Woringer [2] made a preliminary report on this condition, which they termed "lipomelanotic reticulosis", and in 1937 they published a detailed study [3] of this disorder, which has been observed in conjunction with a variety of dermatoses This entity can best be described as lymphadenopathy characterized by proliferation of reticular cells, phagocytosis of fat and melanin and pleomorphic cellular infiltrations

In 1941 Soloff [4] reported the occurrence of this specific alteration of lymph nodes in a case of acute miliary tuberculosis However, in this case it was clearly established that the lipomelanotic changes were not associated with the tuberculosis but had arisen consequent to an intensely pruritic, chronic-recurrent, occupational dermatosis of the groins Subsequent reports have emphasized the association of lipomelanotic reticulosis with some types of lymphoblastoma, as well as with a variety of diverse pruritic dermatoses, such as arsenical exfoliative dermatitis, chronic lichenified eczema, prurigo, seborrheic derma-

From the Department of Dermatology and Syphilology, University of Southern California School of Medicine

1 Jadassohn, J Ueber die Pityriasis rubra (Hebra) und ihre Beziehungen zur Tuberculose (nebst Bemerkungen uber Pigmentverschleppung aus der Haut), Arch f Dermat u Syph **23** 941-979, 1891

2 Pautrier, L M, and Woringer, F Note préliminaire sur un tableau histologique particulier de lesions ganglionnaires accompagnant des éruptions dermatologiques generalisées, prurigineuses, de types cliniques différents, Bull Soc franç de dermat et syph **39**·947-955, 1932

3 Pautrier, L M, and Woringer, F Contribution à l'etude de l'histophysiologic cutanée À propos d'un aspect histo-pathologique nouveau du ganglion lymphatique, La reticulose lipo-melanique accompagnant certaines dermatoses generalisées, Les echanges entre la peau et le ganglion, Ann de dermat et syph 8 256-273, 1937

4 Soloff, L A Lipomelanotic Reticular Hyperplasia of Lymph Nodes Report of a Case, J Lab & Clin Med **27**·343-346, 1941

Charpy [5] stressed the importance of alcoholic solution of calciferol, although the experiences of others indicate that other solvents are just as satisfactory

The addition of calcium to the therapeutic regimen is fairly well accepted in the French reports, although Feeny [4] in England stated the belief that the average diet contains sufficient calcium He maintained that the nutrition of the French people was deficient in calcium during the war and that therefore supplementary amounts were necessary Only one investigator reported no striking benefit from vitamin D_2 therapy [8]

The mode of action is unknown Tomlinson [9] reported that in 3 cases studies of the calcium content made on specimens of tissues obtained from healed lupus skin and from normal skin showed a considerable increase in calcium content of the healed skin, as compared with the normal tissue Charpy [5] advanced the speculation that the liberation of the phosphate ions into the skin is the effective mechanism It is beyond the scope of this paper to enter into further theoretic discussion of this matter

An intriguing and baffling observation in connection with treatment is that though lupus vulgaris is helped remarkably, pulmonary involvement may become activated [10] Fortunately, this development does not occur regularly (case 2)

One additional point is in order In the concept of cutaneous tuberculosis a wide range of lesions and some disputed cutaneous entities are included It would be going too far afield for us to evaluate vitamin D_2 therapy in all these entities Reports on evaluation of this therapy in actual or alleged cases of cutaneous tuberculosis are gradually appearing in the literature [11] This report confines itself to the use of calciferol in lupus vulgaris only

Since there is potential danger in the misuse of this treatment, a discussion of the toxic symptoms is advisable Since benefits of treatments are thought of in long range effects, these toxic symptoms will be divided into reversible (minor) and irreversible (serious) reactions The reversible symptoms include nausea, vomiting, gastrointestinal discomfort, anorexia, occasional diarrhea, mental depression, headache,

8 Aitken, R, in Discussion on Vitamin D in Cutaneous Tuberculosis, Lancet **2** 398 (Sept 13) 1947

9 Tomlinson, K M, in Discussion on Vitamin D in Cutaneous Tuberculosis, Lancet **2** 398 (Sept 13) 1947

10 Macrae,[2] Tomlinson [9] Dowling, G B, in Discussion on Vitamin D in Cutaneous Tuberculosis, Lancet **2** 398 (Sept 13) 1947

11 Fromer and Piacente,[7] Michelson and Steves,[1] Priest, R E Treatment of Endonasal and Cutaneous Lupus Vulgaris with Calciferol Report of a Successful Case, Laryngoscope **58** 305 (April) 1948

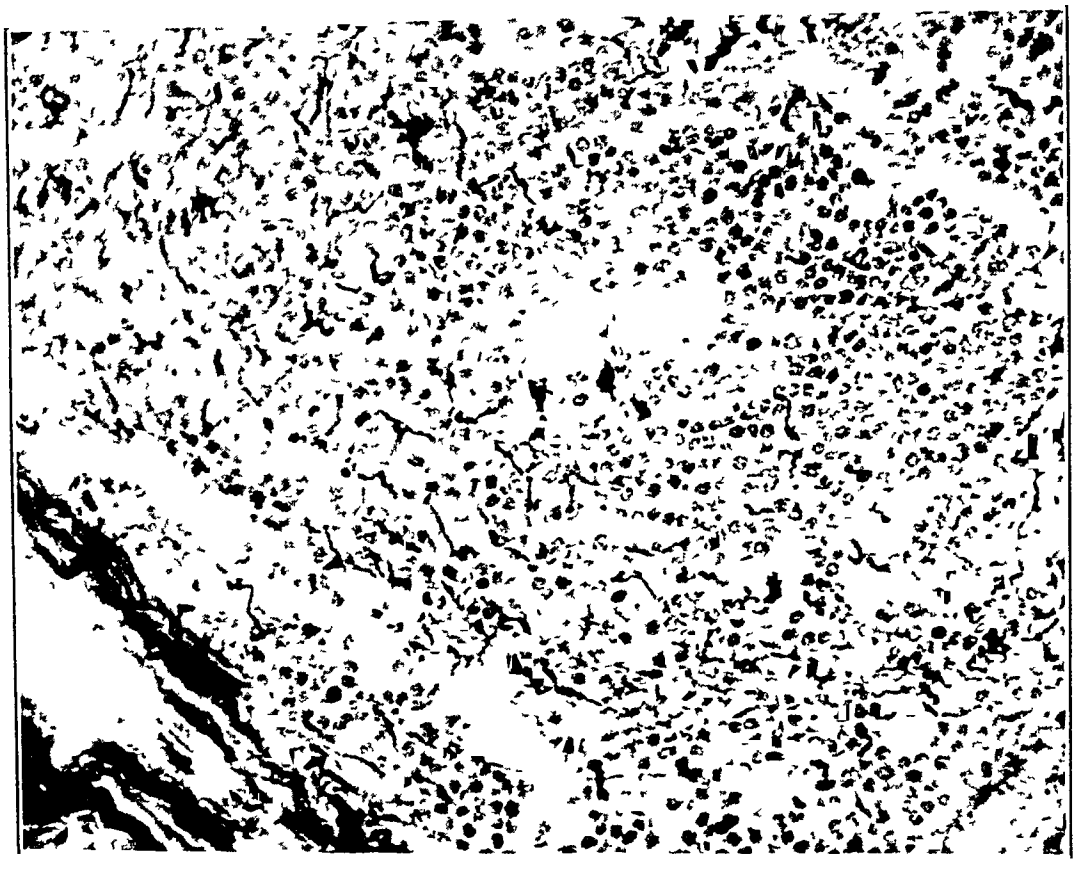


Fig 2—Reticular pattern of hyperplastic lymph node in lipomelanotic reticulosis (reticulum stain, × 38 6)

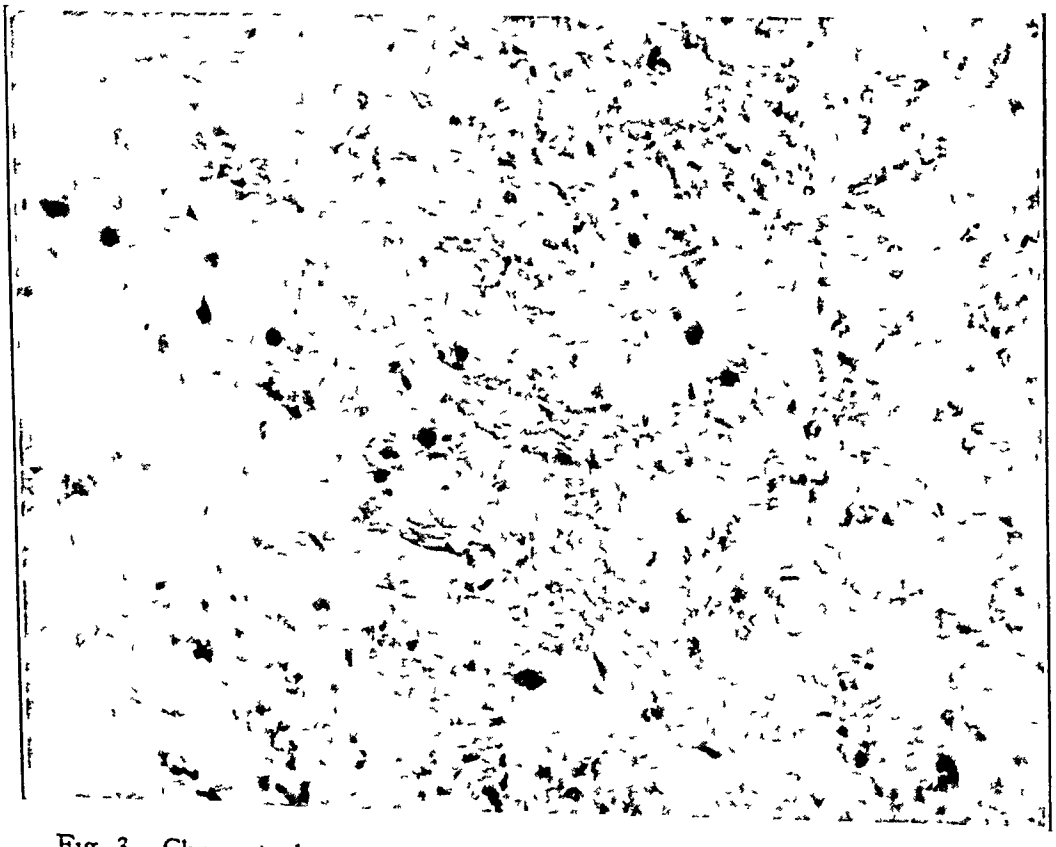


Fig 3—Chromatophores in lipomelanotic reticulosis (silver stain, × 220)

REPORT OF CASES

CASE 1.—M. C., a Negro woman aged 21, was first seen by us on Jan. 20, 1947. She stated that at the age of 7 she had noticed a pinhead-sized lesion on the tip of her nose. This had slowly enlarged, and after about two years ulceration took place. Soon thereafter other nodules appeared, and the glands of the neck became enlarged. Over the intervening years new nodules appeared, in association with periodic swelling of the glands of the neck. The patient stated that numerous roentgenograms of her chest had showed no abnormalities.



FIG. 2 (case 1).—Showing acanthosis, hyperkeratosis and infiltration consisting of lymphocytes, epithelioid cells and Langhans' giant cells, × 120.

Previous treatment had consisted of "sanatorium rest cure" and various local medications. There had been some improvement with rest after several months, but the eruption became worse soon after the patient's discharge from the hospital.

On physical examination the patient was seen to have multiple areas of ulceration on the face (fig. 1*A*). There was appreciable destruction of the nose, multiple deep ulcerations of the nasolabial folds and the lips and one area of ulceration of the inner canthus of the right eye extending partially into the eye.

primary causative factor and the proliferative changes in the lymph nodes secondary, it is not clear why this peculiar hyperplasia occurs in only a small proportion of cases of the various dermatoses in which it has been observed

The frequent occurrence of lipomelanotic reticulosis in patients with cutaneous lymphoblastoma or a precursor of it has sometimes led to the erroneous assumption that the changes in the lymph nodes are part of the malignant process, in fact, the pattern may simulate that of Hodgkin's disease to a remarkable degree However, it has been proved beyond doubt [8] that the lipomelanotic process is only a concomitant of the lymphomatous lesion Nodes may exhibit a lymphoblastic process and lipomelanotic changes at the same time

SUMMARY

The occurrence of lipomelanotic reticulosis of lymph nodes in a case of lichen planus is reported This peculiar lymphadenopathy is associated with chronic pruritus and scratching No adequate explanation has been advanced for its occurrence in only a small proportion of the instances of the various dermatoses with which it is known to be associated

3875 Wilshire Boulevard (5)

8 Lapply,[7] Montgomery, H, and Watkins, C H Monocytic Leukemia Cutaneous Manifestations of the Naegeli and Schilling Types, Hemocytologic Differentation, Arch Int Med **60** 51-63 (July) 1937

only a small ulcerated area persisted on the upper lip Six weeks later, on reexamination, there was still slight crust formation, and the patient was placed again on treatment for two months During this time no toxic symptoms were noticed The urine was normal on repeated examinations, and studies of the blood calcium showed normal amounts Six months after the second course of treatment all the lesions had completely involuted and all signs of activity, including the indurated masses in the submental and anterior cervical regions, were gone Twenty months after the second course of treatment the patient was reobserved, no signs of activity were present then (fig 1 *B*)

CASE 2—M W, a Negro girl aged 15, was first seen by us on Oct 12, 1947 She stated that two years previously she had noticed small nodules on the left cheek and on the nose These had gradually increased in number and in size, and many of them ulcerated and discharged pus All previous treatment had consisted of local applications, during which the process extended

The past history revealed pulmonary tuberculosis, established by identification of M tuberculosis in the sputum

Examination of the skin revealed several ulcerated areas closely confluent, involving a surface of about 5 cm in diameter on the left cheek The borders of the lesion were indurated and the centers covered with a purulent, hemorrhagic crust On the nose there were multiple small nodules but no ulceration These nodules did not completely blanch on diascopic pressure There was pronounced cervical adenopathy

Report on Biopsy—The epidermis was thickened and formed anastomosing rete pegs The dermis showed congestion, edema, small areas of hemorrhage and focal infiltration of lymphocytes and neutrophils One area contained a circular group of epithelioid cells and lymphocytes This lesion resembled an early tubercle The diagnosis was chronic dermatitis, probably tuberculosis

Cultures from the tissue grew no organisms A roentgenogram of the chest showed mottled infiltration radiating from both hilar regions throughout the midportion of the lung fields No cavitation was present

Course—The patient was started on treatment with calciferol (drisdol®) in October, the treatment consisting of 150,000 units per day in addition to 1 quart (0 95 L) of milk Within one week the lesions showed some signs of involution, and within three weeks most of the drainage had ceased Within six weeks of treatment the lesion was completely dry Interestingly enough the use of milk was discontinued for the next few weeks, and it was thought by several independent observers that the rate of involution was slower than usual Milk was reintroduced into the diet and calciferol continued till January 1948, at which time the lesion was 90 per cent involuted

Although the patient showed no toxic symptoms the blood calcium content in January 1948 was reported as 12 5 mg per hundred cubic centimeters Repeated urinalyses revealed normal urine Roentgenologic study revealed no essential change in the pulmonary findings When the patient was seen three months after treatment, involution had proceeded even further, and only a few nodules persisted When she was seen twelve months later, the eruption appeared clinically inactive

CASE 3—S G R, a Negro aged 20, was first seen by us on May 5, 1948, at which time he stated that he had lesions of the face of six months' duration These had begun as small "lumps," which later became ulcerated and discharged considerable amounts of thick pus Previous local treatment had been ineffective

hospitalization was necessary, as all other forms of treatment had failed The average duration of these cases was nineteen years His schedules varied as follows In 7 cases the patient received 600,000 units of calciferol twice weekly, in 7, the calciferol was in an oily solution, in capsule form, and in 6, it was given in emulsion form, the dose being 150,000 units per day During the first two weeks, in practically all cases, the condition became worse After the third week improvement began In 14 cases the patients were discharged clear of lupus lesions, in 3 others they were much improved

Charpy,[5] one of the original proponents of this therapy, advised 15 mg of vitamin D_2 (1 mg of vitamin D_2 is equal to 40,000 units) in alcoholic solution twice weekly for four weeks followed by the same doses for periods varying from two months to two years He stressed that this treatment should be accompanied with 1½ pints (710 cc) of milk daily, plenty of meat, fruits and vegetables Fats should be taken sparingly and the intake of salt reduced Charpy expressed the belief that the good effects should be apparent within fifteen days If no improvement took place, failure of absorption or of tissue permeability should be suspected In successful cases there is no doubt of the clinical benefit, although anatomic cure is more doubtful

Dowling and Thomas[3] stated that calciferol will effect a cure in most cases Treatment should be intensive for three months and carried on possibly for six to twelve months They used a schedule of 150,000 units daily Total doses varied from 9,500,000 units to 62,500,000 in adults, and 4,500,000 to 33,000,000 units in children

Hohmann and Beening[6] reported good results without exception in 87 cases in which a schedule of 90,000 units daily for the first week, and 150,000 units daily for three months thereafter, was used

Fromer and Piacente[7] employed the following schedule 300,000 units every other day for the first week, 200,000 units every other day for the second week and from 50,000 to 100,000 units every day thereafter

Other schedules have been suggested, these do not vary significantly from the aforementioned ones All schedules have been geared to achieving maximum safe doses without significant toxicity

5 Charpy, J Massive Doses of Vitamin D_2 in Therapy of Cutaneous Tuberculosis, Ann de dermat et syph **6**.310 (May-June) 1946, Arztl Monatshft **2** 579 (June) 1946

6 Hohmann, W J, and Beening, G W Massive Doses of Vitamin D_2 in Therapy of Lupus Vulgaris, Nederl tijdschr v geneesk **91**:78 (Jan 11) 1947

7 Fromer, J L, and Piacente, S Vitamin D_2 (Calciferol) in Cutaneous Tuberculosis Report of Seven Cases, Lahey Clin Bull **5** 232 (April) 1948

Numerous roentgenologic examinations of the chest revealed no abnormalities Cultures grew no organisms, observations on urinalysis were repeatedly normal Serologic tests for syphilis revealed low positive titers of 2 to 4 Kahn units on several occasions Examination of spinal fluid on June 6 showed no abnormalities

Course—Because of the history of previous inadequately treated syphilis the patient was given penicillin therapy consisting of 50,000 units every two hours for thirteen days, beginning on May 5 This therapy had no effect on the lesions On May 21, the patient was placed on calciferol therapy and also given 1 5 Gm of calcium gluconate He received this treatment until June 13 On

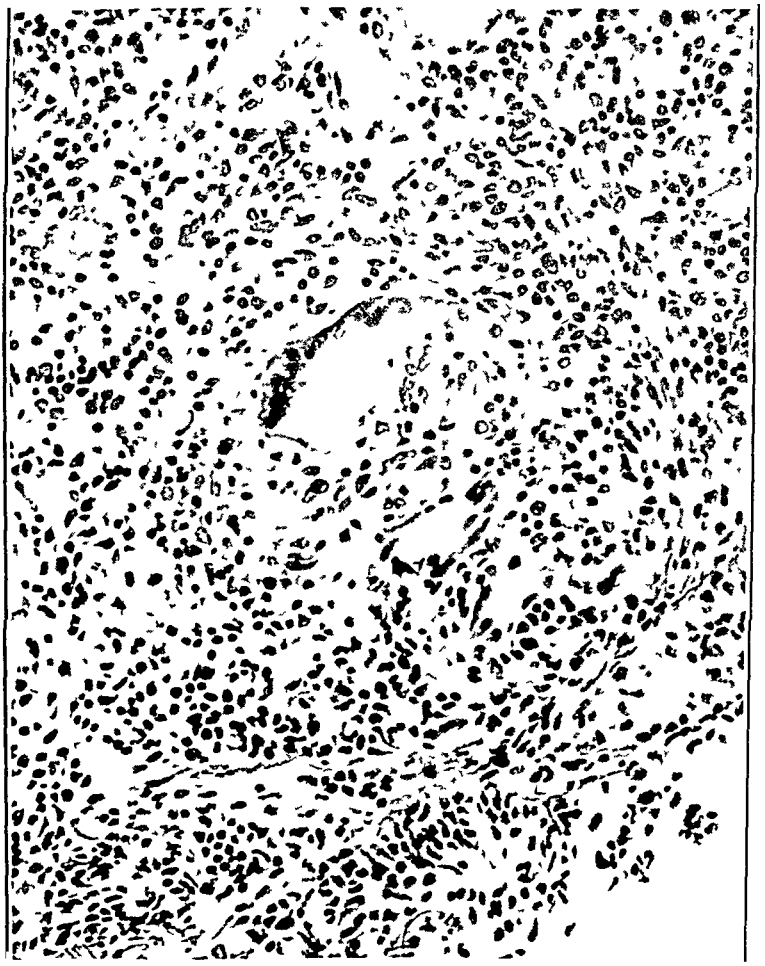


Fig 5 (case 3)—Showing lymphocytes, plasma cells, Langhans' giant cells and epithelioid cells in tubercle formation × 600

that date his temperature was elevated to 102 F This elevation persisted intermittently for several days The patient began to complain of pain in the right lumbar region, radiating to the right shoulder There was no cough or sputum formation The blood calcium on June 9 was 12 mg and on June 10 11 5 mg per hundred cubic centimeters Repeated daily urinalyses were normal at this time The white blood cell count was 22,000, with polymorphonuclear cells, 81 per cent, lymphocytes, 15 per cent, and eosinophils, 4 per cent

The patient was sent to the Eastern North Carolina Sanatorium for further study No evidence of tuberculosis other than the cutaneous lesions could be

giddiness, abnormal tiredness, some frequency of urination in association with transient albuminuria, Herxheimer-like flareup (Macrae [2]), neuralgia along the course of the mandibular nerve, tenderness of the gums and teeth and tingling of the extremities

Macrae [2] reported two unusual reactions beginning with lacrimal and nasal discharge Treatment was stopped immediately, but for the next three weeks symptoms were progressive The patients became drowsy, and thereafter they manifested peripheral neuritis and went into coma The systolic blood pressure dropped, and in 1 instance Cheyne-Stokes respiration developed Both patients recovered completely Interestingly enough, in 1 case the lupus lesions disappeared com-



Fig 1 (case 1) —*A*, showing multiple areas of ulceration on the face *B*, the patient as observed twelve months after the second course of treatment

pletely during the toxic phase Another unusual reversible reaction is reported in our case 3

Metastatic calcification is the serious (irreversible) reaction which limits the dosage scheme Fromer and Piacente [7] expressed the belief that frequent determinations of blood calcium and studies of non-protein nitrogen at regular intervals would keep this incidence down to a minimum Michelson and Steves [1] stated the opinion that subjective symptoms were the most valuable index of tolerance or intolerance The concomitant administration of calcium and phosphorus and exposure to solar or ultraviolet rays augment the effect of vitamin D and may render it more toxic In most carefully controlled cases reported this reaction did not occur

Clinical Notes

A STRANGE CASE OF PALATITIS

HERBERT RATTNER, M D
CHICAGO

A NEW clinical experience is always stimulating and as such should be shared with one's colleagues It is in that spirit that I record the following case

For quite some time I had been observing a comely young woman for soreness of the roof of the mouth Although never severe, it was at all times bothersome, particularly so during the menstrual periods when invariably the symptoms were aggravated Examination showed that her complaint was due to an inflammatory patch on the hard palate—a rather well circumscribed patch about 3 cm in diameter, slightly edematous, and studded with punctate hemorrhages It was only slightly tender to touch

I had never before observed a lesion quite like it, nor could I fit it into any definite dermatologic category—except to suspect that it was due to irritation of some sort The history, however—and a rather exhaustive history, I thought—failed to reveal any clews Then, too, the clinical exacerbations coincided each time with the onset of menses Throughout this period she was also in frequent consultation with her internist for a train of symptoms which he considered were due to psychosomatic rather than to organic disease, for complete and repeated laboratory studies, roentgenologic and clinical examinations had failed to reveal anything abnormal other than the inflammatory patch on the palate

Treatment with a soothing preparation for use as a mouthwash, a diet of bland and soft foods and sedation afforded only slight relief Hormonal therapy, instituted on an empiric basis, was also without benefit A clinical test ruled out the possibility of a fixed drug eruption, and, finally because the case had taxed whatever ingenuity I could muster, it was suggested that a biopsy be performed with the hope that a histologic study would be of some help The young woman overheard the suggestion to her physician and heard me repeat that I still held the opinion that the lesion was a simple inflammatory reaction such as might result from trauma It was then—when the term "trauma" was used instead of irritation—that she asked whether the lesion might not be due to fellatio, only she spoke in the vernacular The menstrual exacerbations? She had practiced the art only during the menstrual periods

The biopsy, of course, was deferred and subsequent events proved how right she was The lesion healed in due course, and then, possessed of a highly developed sense of curiosity—she actually reproduced the lesion

I have since wondered on many occasions whether to be proud of or chagrined at my naivete and failure to solve the case until I encountered a zestful report in the French literature of another case which had similarly puzzled the physician It is quoted in Ronchese's interesting monograph, "Occupational Marks"[1] In my patient, however, the lesion was avocational—I believe

104 South Michigan Avenue

1 Ronchese, F Occupational Marks and Other Physical Signs A Guide to Personal Identification, New York, Grune & Stratton, Inc, 1948 p 167

socket The conjunctivas were decidedly injected The borders of the ulcerative lesions were indurated In the submental region there were subcutaneous masses but no ulceration or drainage

The report on biopsy revealed the following data The epidermis showed hyperkeratosis and acanthosis The underlying tissue was extremely infiltrated with lymphocytes and showed dilated vessels, especially in the most superficial stratum There were a large number of giant cells of the Langhans type and occasionally indistinct, nodular accumulations of pale epithelioid connective tissue cells The diagnosis was lupus vulgaris (figs 2 and 3)



Fig 3 (case 1) —Same section as in fig 2, lower right corner, showing the cells in tubercle formation, × 600

Culture of the discharge and of portions of the tissues taken from the edge of the lesions produced a growth of Mycobacterium tuberculosis on the Petronani medium

Course—On February 2, the patient was placed on a regimen of 150,000 units of calciferol (drisdol®) per day In addition she was given 1 5 Gm of calcium gluconate per day Within one month there was a 50 per cent improvement Treatment with calciferol was continued until June 14, at which time

which occurrences may be attributed to the urethane therapy The clinical and hematologic responses to urethane therapy are reported in detail elsewhere[4]

REPORT OF A CASE

H G, a 76 year old white man, was admitted to the hospital because of the appearance and rapid growth of three tumors about the face and forehead and a fifteen year history of massive, progressive enlargement of masses in the cervical, axillary and inguinal regions The patient was well developed, fairly well nourished and not particularly uncomfortable On one side of the nose there was an elevated, ulcerated lesion 1 5 cm in diameter, with a pearly circular border (figure, *1*) Over the left temporal region there was a papillary mass 4 cm in diameter, with a completely ulcerated and hemorrhagic surface (figure, *1*) Over the right temporal region there was an indurated, fungating tumor 3 cm in diameter, in the center of which was a small superficial ulcer (figure, *2*) There were matted lymph nodes in both sides of the neck Axillary, inguinal and supraclavicular nodes varied from 2 to 5 cm in diameter The edge of the liver was 4 cm below the right costal margin, and that of the spleen was at the level of the iliac crest The tumors of the skin over the left temporal region and near the nose were removed surgically, and the large tumor over the right temporal region was subjected to biopsy All three neoplasms proved to be squamous cell carcinoma Biopsy of an axillary lymph node and study of the blood and bone marrow established the diagnosis of chronic lymphatic leukemia

Oral urethane therapy was started with 3 Gm doses daily Two weeks after onset of treatment the patient began to experience anorexia, but there was no nausea or vomiting After the patient had received 71 Gm of urethane, the leukocyte count, which had been originally 126,500 per cubic millimeter, became less than one-third its initial value There was a reduction in the sizes of the enlarged lymph nodes and spleen The dose of urethane was increased to 6 Gm per day, and this amount was well tolerated After 191 Gm of urethane had been administered, vomiting occurred after ingestion of the drug This was obviated by reducing the dose to 3 Gm daily

During the first fourteen days of treatment a circular zone of hyperemia appeared in the skin around the edge of the tumor in the right temporal region After 107 Gm of urethane had been given, a small area of necrosis developed in this tumor at the site of the incision made when the specimen had been removed for biopsy As treatment was continued, the necrosis extended until it ultimately involved the entire surface of the tumor The superficial one third to one half of the tumor sloughed off In the meantime there was no lateral extension of the lesion (figure, *3*) Successive biopsies revealed changes in the histologic appearance of the tumor, as described later Treatment was discontinued after 221 Gm of urethane had been given because the patient refused further hospitalization The residual portions of the cutaneous tumor were removed surgically before the patient left the hospital Three weeks after therapy had been discontinued the patient died of coronary thrombosis

4 Berman, L, and Axelrod, A R Effect of Urethane on Malignant Diseases Clinical, Hematologic and Histologic Observations on Patients with Carcinoma Leukemia and Related Diseases [case 6], Am J Clin Path **18** 104-129, 1948

The patient also stated that in 1944 he had had an anterior cervical adenitis, for which he had been treated at the Johns Hopkins Hospital He had been told that this condition was tuberculous The adenopathy had subsided in about three months, with considerable scar formation

Early in 1948 he had been told by a physician that he had secondary syphilis He had been given five intravenous injections at the time

On examination the patient was seen to have several areas of ulceration on the inner canthus of the eyes, extending medially to the bridge of the nose



Fig 4 (case 3)—Showing infiltration consisting of lymphocytes, occasional Langhans' giant cells and epithelioid cells, × 120

There were two similar lesions of the right cheek The borders of the ulcerations were quite indurated, and those of the inner canthus extended partly into the eye socket

Report on Biopsy—The skin showed decided acanthosis and hyperkeratosis of the epithelium In the underlying tissue there were nodules consisting of giant cells with peripheral arrangement of the nuclei and a number of epithelioid cells Some of the giant cells presented vacuoles There were numerous lymphocytes and occasional plasma cells in the surrounding area (figs 4 and 5)

The diagnosis was lupus vulgaris

Histologic Study—Biopsy of a specimen taken from the edge of the tumor before treatment began showed the growth to be a well differentiated squamous cell carcinoma with pronounced cornification of the epithelial masses The advancing margin of the tumor was composed of irregular masses of epithelial cells in squamous arrangement with relatively less cornification The tumor infiltrated and replaced the connective tissue of the derma There was little evidence of reaction in the adjacent connective tissue, which was infiltrated with small lymphocytes (figure, *4*) There were a few small leukemic nodules in the outer portions of the derma beneath the normal squamous epithelium The second specimen was obtained after 221 Gm of urethane had been administered The advancing margin of the tumor was broken up into irregular small masses of epithelium separated by abundant, recently formed connective tissue stroma The stromal reaction extended slightly beyond the edge of the tumor (*figure, 5*)

COMMENT

The low incidence of the association of leukemia with other malignant changes was noted by Schreiner and Wehr,[3e] who observed only 4 such cases among a total of 11,212 cases of malignant conditions, including 90 cases of leukemia

The association of chronic lymphatic leukemia with carcinoma of the skin appears to be greater than would be anticipated, as was pointed out by Engelbreth-Holm [1]

The change in the histologic appearance of the squamous cell tumor, characterized by the development of abundant, newly formed fibroblastic stroma, appeared unusual for this type of tumor and was similar to the change produced by urethane in the structure of the Walker rat carcinoma Haddow and Sexton [5] reported that under the influence of urethane the characteristic cellular texture of the Walker carcinoma gave place to a more fibrous structure, with spindle cells and a distinctly more abundant stroma They expressed the opinion that the change was due in part to involvement of vessels and stroma For these reasons we consider the similar alteration in the squamous cell carcinoma of the skin a possible effect of urethane

SUMMARY

A case of multiple squamous cell carcinoma of the skin associated with chronic lymphatic leukemia is reported In the course of urethane therapy degenerative changes were noted in a squamous cell carcinoma of the skin These were characterized by necrosis, with sloughing of the superficial part of the tumor and a decided increase of the fibroblastic stroma without lateral extension of the mass The possible relation between these changes and urethane therapy is discussed

Wayne University College of Medicine

5 Haddow, A, and Sexton, W A Influence of Carbamic Esters (Urethanes) on Experimental Animal Tumours Nature, London **157** 500-503, 1946

established by physical examination and by roentgenologic studies The febrile reaction subsided after several days The cutaneous lesions continued to involute, so that by August 19 they were regarded as completely healed Because of this unusual reaction no further calciferol will be given unless reactivation takes place The possibility of a delayed reaction to penicillin was not completely eliminated

COMMENT

A review of 3 cases of lupus vulgaris in which calciferol (vitamin D_2) therapy was used indicates that this form of treatment is probably one of the most effective for this infection That it is not free from potentially serious reaction is self evident Moreover, it must be used with caution in the presence of active pulmonary tuberculosis

A word of discussion concerning streptomycin is in order While both streptomycin [12] and calciferol are effective remedies, the eventual choice of one or the other forms of treatment will depend primarily on which produces more serious toxic irreversible reactions in therapeutically effective schedules Other minor factors, such as the cost of treatment, its duration and the need for hospitalization, may have to be considered Hospitalization is not necessary with calciferol therapy The optimum dosage, which will produce the best therapeutic results with the least toxicity has not been established for either streptomycin or calciferol Possibly a combination of both forms of therapy may be additive or synergistic,[13] thereby combining the desired therapeutic advantage with reduction of dose and toxicity As a rule, in the presence of concomitant pulmonary tuberculosis the use of streptomycin should precede that of calciferol in the treatment of cutaneous tuberculosis

CONCLUSIONS

1 Vitamin D_2 (calciferol) in doses of 150,000 units per day caused involution of lesions in 3 cases of lupus vulgaris

2 Supplementary treatment with calcium may enhance this effect

3 In the presence of active pulmonary tuberculosis this medication should be used cautiously That the presence of active pulmonary tuberculosis is not an absolute contraindication to the use of vitamin D_2 is supported by the report of case 2, in which no flare-up of proved pulmonary tuberculosis took place under active treatment with calciferol

4 Careful, repeated examinations should be made during the course of therapy for serious (irreversible) effects of metastatic calcification

708 Medical Arts Building (10)

12 O'Leary, P A , Ceder, E T , Hinshaw, H C , and Feldman, W H · Treatment of Various Types of Cutaneous Tuberculosis with Promizole and Streptomycin, Arch Dermat & Syph **55** 222 (Feb) 1947

13 Cornbleet, T Combined Calciferol and Streptomycin in Lupus Vulgaris, J A M A **138** 1150 (Dec 18) 1948

2 Pruritus associated with systemic diseases, such as diabetes mellitus and jaundice Treatment of the underlying systemic disease will help control the pruritus

3 Pruritus due to allergy and caused by release of histamine or H substance in the tissues In this group are urticaria, atopic dermatitis and contact dermatitis, as well as localized neurodermatitis and localized areas of pruritus Only H substance–mediated pruritus is considered in this report

Oral use of antihistaminic agents for various forms of allergy is now well established [2] Although the therapeutic action of these agents is purely palliative, they afford significant symptomatic relief In the cutaneous manifestations of allergy, peroral antihistaminic therapy has been found particularly useful for symptomatic control of itching incident to urticaria, atopic dermatitis and contact dermatitis

It has been demonstrated by other workers in the field of allergy [3] that local application of a solution of an antihistaminic agent produces significant reduction in the whealing reaction produced by application of histamine to the skin However, oral administration of the antihistaminic agent has but a slight inhibitory effect on experimentally produced histamine wheals This observation suggests that local application of an antihistaminic substance should be more effective than oral administration in inhibiting histamine wheals

Wheals resulting from an antigen-antibody reaction, such as those occurring in persons sensitive to ragweed, are similarly inhibited by local application of a solution of an antihistaminic agent This fact would suggest that the antigen-antibody reaction leads to release of histamine in the tissues and that antihistaminic solution inhibits the effects of histamine

The mode of action of antihistaminic agents is not definitely known Several theories have been proposed that they prevent the release of histamine in tissues, that they neutralize histamine and that they block the action of histamine The last theory is accepted by most authorities It is claimed that the antihistaminic drug combines with the tissue cells at the site of action of the histamine rather than with the histamine itself Thus, the pharmacologic effects of histamine are prevented by blocking the union of histamine with the tissue cells

With these considerations in mind, it was felt that incorporation of diphenhydramine hydrochloride (benadryl hydrochloride®), an antihistaminic agent, in an ointment would permit concentration of this therapeutic agent in the epidermis, where its histamine-blocking powers would be of great value Symptoms resulting from allergic release of histamine in the tissues, such as pruritus and exudation of fluid, might thus be controlled or eliminated [4]

Another advantage from the local application of an antihistaminic agent, in the form of diphenhydramine hydrochloride ointment, would be elimination of systemic side actions, such as drowsiness and nausea, that may accompany the oral administration of antihistaminic substances

2 Levin, S J β-Dimethylaminoethyl Benzhydryl Ether Hydrochloride (Benadryl) Its Use in Allergic Diseases, J Allergy **17** 145 (May) 1946

3 Friedlaender, S, and Feinberg, S M Histamine Antagonists III The Effect of Oral and Local Use of β-Dimethylaminoethyl Benzhydryl Ether Hydrochloride on the Whealing Due to Histamine, Antigen-Antibody Reactions, and Other Whealing Mechanisms Therapeutic Results in Allergic Manifestations, J Allergy **17** 129 (May) 1946

4 Feinberg, S M and Bernstein, T B Tripelennamine ("Pyribenzamine") Ointment for the Relief of Itching, J A M A **134** 874 (July 5) 1947

MULTIPLE SQUAMOUS CELL CARCINOMA OF THE SKIN ASSOCIATED WITH CHRONIC LYMPHATIC LEUKEMIA

Observations on the Effect of Urethane Therapy

ARNOLD R AXELROD, M D
AND
LAWRENCE BERMAN, M D
Detroit

In 1941 Engelbreth-Holm[1] reviewed 22 cases of leukemia associated with other malignant conditions and added reports of 11 cases of his own Since then 13 additional cases[2] of leukemia combined with various types of malignant diseases have been reported

Of the 46 cases reported, carcinoma of the skin was associated with the leukemia in 14[3] Basal cell carcinoma was reported in 8 and squamous cell carcinoma in 6 of the cases Chronic lymphatic leukemia was noted in each of the 14 cases

We have observed a patient who exhibited multiple squamous cell carcinoma of the skin associated with chronic lymphatic leukemia We report this case because of apparent rarity of the combined malignant conditions and also because this patient received urethane therapy and showed clinical and hematologic response, as well as definite changes in a squamous cell carcinoma of the skin,

From the Departments of Medicine and Pathology, Wayne University College of Medicine and the City of Detroit Receiving Hospital

1 Engelbreth-Holm, J Leukemia and Another Malignant Tumor in Same Patient, Nord med (Hospitalstid) **9**.791-799, 1941

2 (*a*) Morrison, M , Feldman, F, and Samwick, A A Carcinoma and Leukemia Report of Two Cases with Combined Lesions, Review of Literature, Ann Int Med **20** 75-84, 1944 (*b*) Dustin, P, Jr Coexistence d une leucemie lymphoide et d'un carcinome gastrique, Rev belge sc méd **13** 199-208, 1941 (*c*) Delcourt, R, and van Vliet, P Coexistence d'une leucemie lymphoide et d'un carcinome, Acta med Scandinav **119** 47-56, 1944 (*d*) Evans, T S , Swirsky, M Y, and Chernoff, H M Primary Endothelioma of the Pleura Report of a Case in a Patient with Chronic Lymphatic Leukemia, Ann Int Med **24** 262-272, 1946 (*e*) Reiss, F, and Konheim, W Basal Squamous Cell Epithelioma Associated with Leukemia, Arch Dermat & Syph **55** 507-511 (April) 1947

3 (*a*) Engelbreth-Holm[1] (*b*) Reiss and Konheim[2e] (*c*) Fuhs, H Multizentrische Basalzellenepitheliome bei lymphatischer Leukamie, Dermat Wchnschr **85** 1533, 1927 (*d*) Scheuffler, A Carcinombildung auf einem Leukamid Arch f Dermat u Syph **168** 586-596, 1933 (*e*) Schreiner, B F , and Wehr, W H Cancer Associated with Leukemia, Am J Cancer **21** 368-371, 1934 (*f*) Pulvertaft, R J V Multiple Primary Epithelioma in Lymphatic Leukemia, Brit J Surg **24** 50-54, 1936

had recurrences of the localized patches of neurodermatitis, either in the same or in new locations, after a lapse of from four to six months

In contact dermatitis, of 51 patients treated, 36 experienced some relief of itching while under treatment with diphenhydramine hydrochloride ointment, while 15 patients showed no improvement or became worse It was found that in cases of acute contact dermatitis, when the skin was highly inflamed, swollen and oozing, the patients complained of a burning sensation when the ointment was first applied This burning sensation usually persisted in the acute cases, and use of the ointment had to be discontinued In the milder and subacute cases of contact dermatitis, the burning sensation was less severe and was usually followed by a sensation of numbness and later by relief of itching It was felt, therefore, that during the acute phase of a contact dermatitis conservative measures, such as wet dressings and soothing lotions and ointments, should be used Later, after the acute phase has subsided, one may apply diphenhydramine hydrochloride ointment In the majority of cases of contact dermatitis, however, the patients experienced considerable relief of pruritus after the application of diphenhydramine hydrochloride ointment

Nummular eczema may be favorably influenced by the use of the ointment, which simply relieves the pruritus but has no effect on the course or progress of the disease itself New patches of nummular eczema or reactivation of healing lesions may occur while patients are under treatment with diphenhydramine hydrochloride ointment

The ointment is also of value in stasis dermatitis It helps to control the pruritus However, unless measures are used to improve the circulation in the legs, the pruritus and excoriations recur when use of diphenhydramine hydrochloride ointment is discontinued

This ointment was found of considerable value in relieving pruritus in a group of patients with pruritus ani, pruritus vulvae and pruritus scroti These conditions are distressing and annoying to the patient, keeping him awake at night The diphenhydramine hydrochloride ointment, therefore, was useful in controlling pruritus in these cases Of course, if the pruritus is due to a local cause, such as a fungous infection, it should be treated accordingly

Diphenhydramine hydrochloride ointment was also used locally in treatment of a group of miscellaneous pruritic dermatoses, such as lichen planus, pityriasis rosea and chronic recurrent urticaria The results were satisfactory in a majority of cases of these conditions, the patients experiencing some relief of the pruritus Diphenhydramine hydrochloride ointment was, of course, used as a purely palliative measure in all the cases

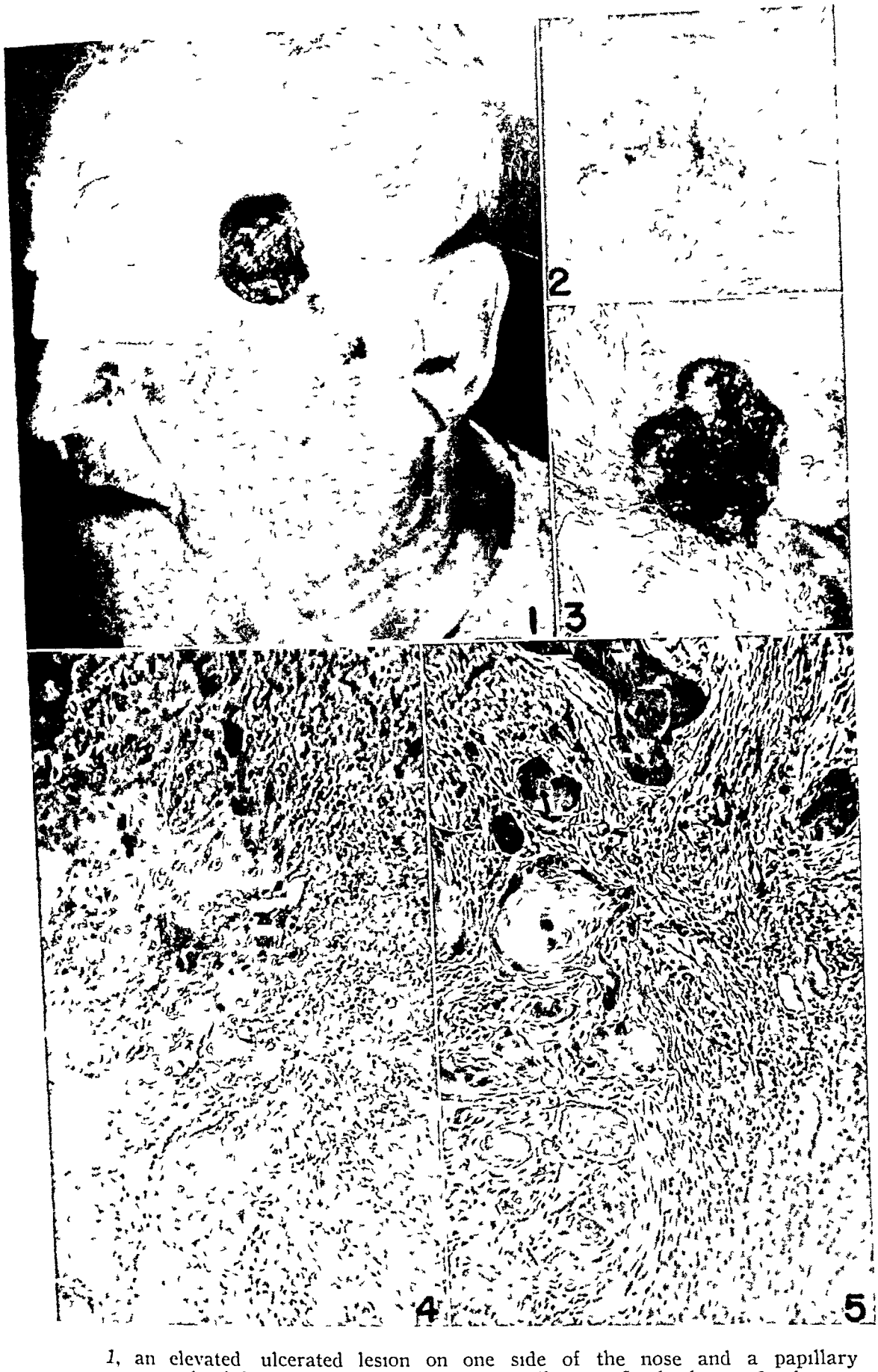
In a small percentage of cases, about 2 per cent of the cases in this series, signs of sensitization or irritation appeared during treatment with the ointment The ointment was, of course, discontinued when signs of irritation developed from its use

SUMMARY

Diphenhydramine hydrochloride ointment is of value for relief of pruritus in a variety of dermatoses

Its action is purely palliative It has no effect on the course or progress of a dermatosis except for relief of the pruritus

Diphenhydramine hydrochloride ointment is worth a trial in all cases of pruritic dermatoses that have either an allergic or a neurogenic background



1, an elevated ulcerated lesion on one side of the nose and a papillary mass over the left temporal region *2*, a small, superficial ulcer *3*, changes observed in the tumor in the right temporal region *4*, photomicrograph of a specimen taken before the beginning of treatment *5*, photomicrograph of specimen obtained after the administration of 221 Gm of urethane

pyridine, 1 Gm twice a day for five days, in order to prevent recurrence Reexamination six weeks later showed the scalp to be entirely free of lesions

CASE 2—*History*—W A E, a married white man aged 50, was seen in the office of Dr John G Downing on May 5, 1947 He complained of numerous lesions scattered over the entire surface of the scalp, these had been present for two months There were no subjective symptoms, and the patient was chiefly concerned with the unsightly appearance of the lesions



Fig 1 (case 1) —Isolated lesion of molluscum contagiosum

Examination—Several hundred semiglobular lesions, varying in size from 1 to 5 mm, were seen scattered over the entire surface of the scalp Some of the lesions were umbilicated, but the majority had a smooth, dome-shaped surface (fig 2) The lesions occurred both singly and in groups, those in groups favoring the parting of the hair The lesions did not extend beyond the hair line The rest of the skin was normal A specimen was removed for biopsy, and the histologic diagnosis was molluscum contagiosum

Treatment and Subsequent Course—Sulfapyridine, 1 Gm three times a day for one week, was administered orally but failed to influence the lesions A 25

AUREOMYCIN IN MOLLUSCUM CONTAGIOSUM

W H GUY, M D
F M JACOB, M D
AND
W B GUY, M D
PITTSBURGH

Experimental work of Wile and Kingery [1] on the etiology of molluscum contagiosum led them to conclude that the disease is due to a filtrable virus Further reports on the value of the drug aureomycin in diseases of the rickettsia-virus group led us to try it on a widespread case of molluscum contagiosum

C S presented himself in our office with a generalized eruption of molluscum contagiosum, with what we estimated to be three hundred lesions on the trunk and extremities There was a history of the appearance of a dozen or so lesions on the trunk at first, and of the condition's becoming generalized a few days after a massage in a Turkish bath A few of the lesions were curetted, more for diagnostic purposes than for any other, because it seemed hopeless to try to treat so many lesions by this method

We prescribed aureomycin, 250 mg twice a day by mouth for two days Four days after treatment with the drug had been stopped, the lesions were almost flat No more aureomycin was prescribed, but white lotion N F was prescribed to be applied locally to hasten the removal of the remaining debris in the lesions In another week nothing was left of the lesions but pigmented macules, and in the following week there was no sign of recurrence

This dramatic response, although in only a single case, seemed to justify calling attention to the possibility of using this drug in molluscum contagiosum and in other conditions presumably of virus origin, such as verruca vulgaris, juvenile flat warts and plantar warts

7026 Jenkins Arcade (22)

From the Department of Dermatology and Syphilology, University of Pittsburgh School of Medicine

1 Kingery, L B Histogenesis of Molluscum Contagiosum, Arch Dermat & Syph **2** 144 (Aug) 1920

CONTROL OF PRURITUS WITH DIPHENHYDRAMINE (BENADRYL®) HYDROCHLORIDE OINTMENT

L ORECKLIN, M D
DETROIT

Pruritus, or itching, is a distressing symptom of many dermatoses In clinical management of pruritus, optimal therapeutic results are predicated on adequate diagnosis of the etiologic factor Briefly, the various types [1] of pruritus may be classified according to cause, under three main headings

1 Pruritus incident to parasitic diseases of the skin, such as scabies and pediculosis Destruction of the parasite by use of suitable antiparasitic agents will automatically clear up the pruritus

1 Klauder, J V Pruritus Considerations on Its Pathogenesis, Pennsylvania M J **37** 729 (June) 1934 Sulzberger, M B, and Wolf, J Pruritus and Its Treatment, M Clin North America **19** 971 (Nov) 1935

AUTOHEMOTHERAPY OF HERPES ZOSTER

Results in One Hundred and Fifty-Four Cases

DUNCAN O POTH, M D
SAN ANTONIO, TEXAS

Spectacular relief of pain following autohemotherapy in herpes zoster was reported by Jack W Jones and Herbert S Alden [1] Cures were obtained with one injection in most cases, and 1 instance is reported in which pain subsided before the patient returned home, 75 miles from Atlanta Jones and Alden did not report the number of patients treated, nor did they report treatment failures

Most textbooks [2] do not mention this type of treatment Instead, a general hodgepodge of remedies is given, these including even the use of cathartics Becker and Obermayer [3] devoted one sentence to autohemotherapy in their textbook

Ravaut [4] introduced injections of whole blood from vein to muscle in 1913 Centrifuged serum had been used prior to this report

Burgess [5] attempted to draw conclusions as to the explanation of the mechanism of action of autohemotherapy However, no clearcut explanation has ever been offered Autohemotherapy has been my routine office procedure to the exclusion of all other treatment Consequently, the results obtained in 154 cases are reported

RESULTS OF AUTOHEMOTHERAPY

Data concerning only those patients with pain and active vesicles are included in this report Asymptomatic persons were not treated Twenty-seven patients received only one injection, 21 received two injections, 77 received three injections, and 16 received four injections

These 141 patients averaged 2 5 injections and obtained complete relief of pain in 5 22 days, although severe pain had usually subsided before the second or third injection was given The youngest patient treated was 4 years and the oldest 82 years of age

1 Jones, J W, and Alden, H S South M J **30** 735 (July) 1937

2 Ormsby, O S, and Montgomery, H Diseases of the Skin, ed 6, Philadelphia, Lea & Febiger, 1943 Sutton, R L, and Sutton, R L, Jr Diseases of the Skin, ed 10, St Louis, C V Mosby Company, 1939 Andrews, G C Diseases of the Skin, ed 2, Philadelphia, W B Saunders Company, 1938

3 Becker, S W, and Obermayer, M E Modern Dermatology and Syphilology, Philadelphia, J B Lippincott Company, 1940

4 Ravaut, P Ann de dermat et syph **4** 292, 1913

5 Burgess, N Brit J Dermat **44** 124 (March) 1932

Accordingly, diphenhydramine hydrochloride ointment, containing 2 per cent of the drug, was employed in management of the following dermatoses in which itching is a prominent symptom neurodermatitis (generalized and localized), contact dermatitis, nummular eczema, stasis eczema, pruritus ani, pruritus vulvae and pruritus scroti

Clinical results are summarized in the accompanying table

COMMENT

In a series of 268 patients with various pruritic dermatoses, 196 had some relief of itching when diphenhydramine hydrochloride ointment was applied locally, while 72 had no improvement In this series, improvement is defined as relief of itching, evaluation being based on the patient's own statement It is not implied that the underlying condition of the skin cleared up as a result of local application of diphenhydramine hydrochloride ointment

Clinical Results with Diphenhydramine Hydrochloride (Benadryl Hydrochloride®) Ointment in Control of Pruritus

Conditions	No of Patients	No of Patients Showing Improvement	No of Patients Not Showing Improvement
Neurodermatitis			
Generalized	32	19	13
Localized	70	58	12
Contact dermatitis	51	36	15
Nummular eczema	22	17	5
Stasis eczema	18	14	4
Pruritus ani	20	15	5
Pruritus vulvae	10	8	2
Pruritus scroti	7	5	2
Miscellaneous dermatoses	38	24	14
Totals	268	196	72

In some cases, the ointment had to be applied every two or three hours in order to control the pruritus With relief of pruritus, there was, of course, decreased scratching and excoriation and less mechanical injury to the skin This situation usually resulted in objective improvement in clinical manifestations of the dermatoses, particularly in cases of localized neurodermatitis and stasis eczema

In neurodermatitis disseminata, or atopic eczema, which is a recurrent, resistant, pruritic dermatosis, there was relief of pruritus for 19 of 32 patients treated However, some of these patients who showed relief of pruritus had exacerbations of the atopic eczema while under treatment with diphenhydramine hydrochloride ointment The ointment apparently had no effect on the course of atopic eczema

In localized neurodermatitis, of 70 patients treated, 58 showed improvement and relief of pruritus These patients can also be classified as having lichen chronicus simplex As is well known, pruritus is an outstanding symptom in this disease, and the patient often scratches himself during the night, thus reactivating the lesions over periods of months and years By relieving the pruritus in these cases, the vicious cycle is broken, and the patient refrains from scratching Lesions of several years' duration have cleared up in from four to five weeks under treatment with diphenhydramine hydrochloride ointment Some patients, however, have

obtained in the 141 patients in this report treated by autohemotherapy It is a simple, effective method of treatment that is completely free of complications, regardless of age or physical condition of the patient

Complete relief of pain was obtained in an average of 5 22 days Severe pain had usually subsided before the second or third injection was given Treatment was given every third day until the patient reported complete relief of pain

Most textbooks do not even mention this type of treatment, and a very complicated surgical procedure, paravertebral procaine block, was reported by Findley and Patzer [6] Combined treatment gave no better results than did autohemotherapy alone

CONCLUSIONS

The results of autohemotherapy in 154 cases of herpes zoster are reported

Cure was obtained in all but 4 cases, and in these the patients subsequently recovered

No reactions or contraindications to treatment were encountered

Autohemotherapy is suggested as a simple routine procedure in the treatment of herpes zoster

1230 Nix Building (5)

6 Findley, T , and Patzer, R Treatment of Herpes Zoster by Paravertebral Procaine Block, J A M A **128** 1217 (Aug 25) 1945

SIMPLE APPARATUS FOR CLINICAL PHOTOGRAPHY

STUART T ROSS, M D
HEMPSTEAD, N Y

There has long been a need for a device by means of which the clinician can take photographs in color of various small lesions about the body without becoming entangled in great expense or cumbersome apparatus The dermatologist, proctologist and general surgeon, especially, should find simplified clinical photography advantageous particularly for teaching purposes

By means of the apparatus about to be described excellent kodachrome® transparencies of any cutaneous lesion, postoperative wound or pathologic condition which appears on the surface may be taken with a minimum of effort and expense

As pictured (fig 1) there is a transverse 15 inch (38 cm) bar of aluminum, square in cross section and hollow, at each end of which is fastened a socket to hold a number 1 photoflood lamp in an ordinary matte reflector Slots are placed as shown to permit the affixion of any camera, although the kodak bantam® is recommended as particularly suited to this work The transverse bar is perforated at a right angle by an 18 inch (45 7 cm) aluminum rod calibrated in inches The position of this rod is adjustable so that the camera may be focused at any predetermined distance from the subject

My practice being limited to proctology, I find that a 5½ by 8 inch (14 by 20 3 cm) field is usually satisfactory and is attained by the use of a number 3

Use of the ointment is contraindicated in denuded and weeping areas because of its burning effect

In diphenhydramine hydrochloride ointment, physicians have another means of controlling pruritus This medication should be of especial assistance to those who treat patients with dermatologic disease

The diphenhydramine hydrochloride ointment, with a 2 per cent concentration of diphenhydramine hydrochloride, used in this study was supplied by Parke, Davis and Company's Department of Clinical Investigation

914 Maccabees Building

MOLLUSCUM CONTAGIOSUM OF THE SCALP

Report of Two Cases

WILLIAM R HILL, M D
Assistant in Medicine and Assistant in Dermatology, Harvard Medical School and Massachusetts General Hospital
AND
SALVATORE J MESSINA, M D
Instructor in Dermatology, Boston University School of Medicine and Assistant Visiting Dermatologist, Massachusetts Memorial Hospitals
BOSTON

White [1] and Nicoletti [2] each reported a case of molluscum contagiosum located exclusively on the scalp, and the latter, after a thorough review of the literature, collected 5 similar cases To this small number the following observations are added

REPORT OF CASES

CASE 1.—*History*—D J, an unmarried white woman aged 55, was first seen by us on Feb 26, 1947 She complained of a small lesion situated on the vertex of the scalp, to the left of the midline, which had been present for several months and had gradually increased in size On several occasions, while combing her hair, she had struck the lesion, causing bleeding This development was followed by moderate tenderness for a few days

Examination.—At the time of the initial visit, a pea-sized, round, waxy nodule with a rolled border and central hemorrhagic crust was observed in the left parietal region A tentative diagnosis of basal cell carcinoma was made The lesion was excised, and the specimen was submitted for biopsy The pathologic diagnosis was molluscum contagiosum

Treatment and Subsequent Course.—One week later, a well circumscribed, semiglobular nodule with a rolled border and depressed central plug was noted 2 cm posterior to the original lesion (fig 1) Microscopic examination of the expressed contents of the lesion revealed molluscous bodies The rest of the skin was normal at that time

This lesion, as well as two small lesions which appeared two weeks later, was destroyed by electrodesiccation The patient was then instructed to take sulfa-

1 White, C Molluscum Contagiosum of the Scalp, Arch Dermat & Syph **21** 180 (Feb) 1930

2 Nicoletti, V Mollusco contagioso localizzato esclusivamente al cuoio capelluto, Arch ital di dermat, sif **6**·194, 1930

News and Comment

GENERAL NEWS

Volume 3 of "Collected Studies of Skin Diseases" Still Available—The Barnard Free Skin and Cancer Hospital has 300 copies of volume 3 of "Collected Studies of Skin Diseases," which was published during the war The hospital was unable to send it to all dermatologists because many of them were in the service at the time of publication The volume is now available, to those who have not received a copy, on request to the hospital, and copies will be mailed on a "first come, first served" basis

Editors of Society for Investigative Dermatology—At the June 1949 meeting of the Society for Investigative Dermatology, Dr Naomi M Kanof was appointed chairman of the editorial board Dr Marion B Sulzberger was named chief editorial consultant Manuscripts and inquiries should be addressed to the Editorial Office at 1150 Connecticut Avenue N W, Washington 6, D C

per cent alcoholic solution of resin of podophyllum was then applied locally This treatment caused great discomfort, without producing beneficial results, and was discontinued after two weeks The lesions were destroyed by electrodesiccation at subsequent visits Examination six months later showed a normal scalp



Fig 2 (case 2) —Multiple lesions with tendency to group formation

SUMMARY AND CONCLUSIONS

Two cases of molluscum contagiosum, in both of which small, discrete, semiglobular lesions were located exclusively on the scalp, are reported Treatment by excision and electrodesiccation produced beneficial results

The occurrence of molluscum contagiosum on the scalp may be more frequent than was formerly suspected and merits consideration in differential diagnosis of tumors of the scalp

520 Commonwealth Avenue

Ranson [4] stated in his text that the nerves of the skin are largely sensory, with a small admixture of sympathetic fibers In a predominantly sensory nerve, like the saphenous nerve in the cat, he found the small trunks to be made up of large myelinated fibers, small myelinated fibers and many small unmyelinated fibers, which outnumber the myelinated ones three or four to one The unmyelinated fibers mediate the sensation of pain, the large myelinated fibers, the sensation of touch, and the small myelinated ones, probably the sense of temperature

I adopted J Gay Prieto's [5] modification of the silver impregnation method of Ramon y Cajal for the demonstration of nerve fibers in the skin This is a block method with the drawback that once the tissue is impregnated no subsequent modification of the coloration

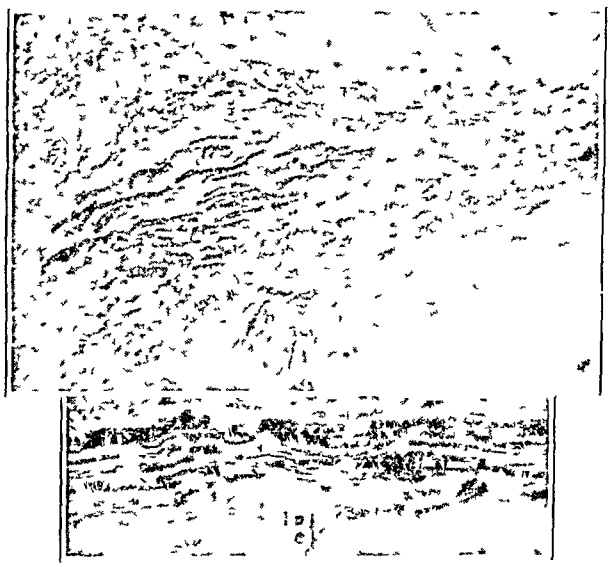


Fig 1.—*A*, bias section of a normal nerve bundle in the midcorium beneath an ulcerated zoster lesion of eleven days' duration Large, medium-sized and very small nerve fibers can be readily seen The very fine nerve fibers are probably nonmyelinated, × 1,000 *B*, a longitudinal section of a nerve bundle from the same section as *A*, × 1,000

is possible It was adopted because of considerable previous experience in its use It makes visible the myelinated fibers, large and small, as well as the unmyelinated fibers (figs 1 and 2) It was considered better than the Marchi stain for showing myelin degeneration because the nonmyelinated fibers outnumber the myelinated in the sensory nerve bundles I know of no method that will distinguish the sensory nerve fibers in a bundle from motor and sympathetic fibers How-

4 Ranson, S W The Anatomy of the Nervous System Its Development and Function revised by S L Clark ed 85, Philadelphia, W G Saunders Company, 1947, p 115

5 Gay Prieto, J Bull Soc franç de dermat et syph **42** 1069-1071, 1935

Injections (10 to 15 cc) were given every third day until relief of pain was reported by the patient Local treatment with solution of boric acid and 2 per cent phenol in calamine lotion was prescribed for most cases Ointment containing dibucaine (nupercaine®) hydrochloride or tetracaine (pontocaine®) hydrochloride was used for hyperesthesia

There were 4 patients who continued to have some degree of pain after autohemotherapy These were given posterior pituitary injection U S P (pituitrin®), a preparation containing the vitamin B complex, sodium iodide and roentgen therapy They became free from pain in seventeen, twenty-six, twenty-seven and thirty-four days

These 4 patients represent less than 3 per cent of the total group treated All showed improvement and no longer complained of severe pain, but, because of residual dull, aching pain, autohemotherapy was stopped Two of the 4 were in severe tension states at the onset of the zosteric pain In fact, it is surprising that I did not encounter enough psychoneurotic persons and "complaining type" of patients in general to make the number of treatment failures run much higher in this series When 141 patients are treated for any medical condition the treatment failures are usually more than 3 per cent simply because some patients refuse to admit a cure

COMBINED TREATMENT

In 1937 posterior pituitary injection was used in conjunction with autohemotherapy A series was started to compare this type of treatment with that with posterior pituitary injection or autohemotherapy alone This combined method was soon discontinued because of reactions and lack of results However, data concerning the small group receiving it are incorporated in this report because all the patients received injections of whole blood on the same schedule as did the larger group

Thirteen patients received pituitrin injections and autohemotherapy These persons were treated daily, receiving injections of whole blood, of from 10 to 15 cc, every third day and 1 cc of surgical pituitrin® (posterior pituitary solution in 1 cc ampuls containing 20 pressor units) on the days between injections of blood All obtained relief of pain in about the same length of time as did patients treated with autohemotherapy alone In this small group there were no treatment failures

REACTIONS TO TREATMENT

The group receiving posterior pituitary injection complained of pain at the site of injection Some nausea and diarrhea were also encountered Pregnancy contraindicates the use of posterior pituitary injection because of the medicolegal aspect in cases of abortion or stillbirth from any cause

The larger group receiving autohemotherapy alone presented no contraindications to treatment A few patients complained of painful hips and sore arms after treatment No instances of chills and fever were recorded

SUMMARY

Autohemotherapy was reported by Jones and Alden to act almost as a specific for the treatment of herpes zoster This statement is substantiated by the results

was good evidence of the disappearance of the majority of the nerve fibers in some of the bundles in the middle and deeper portions of the corium

The scars of former zoster lesions were removed from 3 patients One removed sixty days after the attack (fig 5 *A*) showed reduction of the nerve fibers in some of the deeper bundles In another, removed three hundred days after the eruption (fig 5 *B*), the stain was pale but there was some evidence of nerve degeneration In a third case, tissue removed a year and a half after the attack failed to become impregnated satisfactorily and so was discarded

In a case of herpes zoster generalisatus the site of one of the aberrant vesicles was tattooed and removed forty days later No evidence of nerve degeneration was found

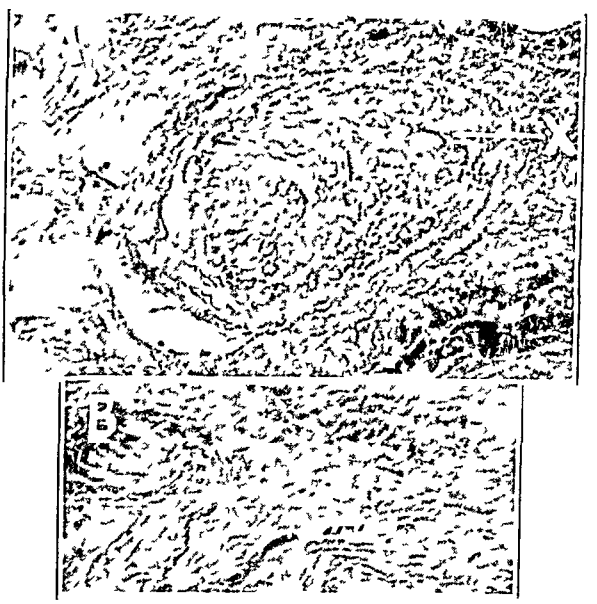


Fig 3—*A*, cross section of a large nerve bundle entering the corium from below in a section taken from a zoster lesion of fourteen days' duration Only a few fibers, such as may be seen at *X*, remain intact, × 1,000 *B*, longitudinal section of a bundle in the midcorium of the same section Only one large and one small nerve fiber are well visualized, × 1,000

A biopsy specimen was taken from normal skin between the zoster lesions in 2 patients One taken on the eighteenth day showed pronounced degeneration of a bundle deep in the corium In another patient, a specimen taken on the eighteenth day after appearance of a brachial zoster in a boy 17 years of age (fig 6), the apparently normal skin between the lesions showed decided diminution in the number of nerve fibers in some of the bundles

When a peripheral sensory nerve fiber is severed from its cell body, either by the death of the ganglion cell or by the interruption of the peripheral axon, wallerian degeneration of the distal portion

Portra® lens at 10 inches (25 cm) In order for the picture to be taken, the apparatus is plugged into an ordinary wall socket, the lights are turned on, the tip of the focusing rod is touched to the skin just below the lesion to be photographed, and the cable release is pressed

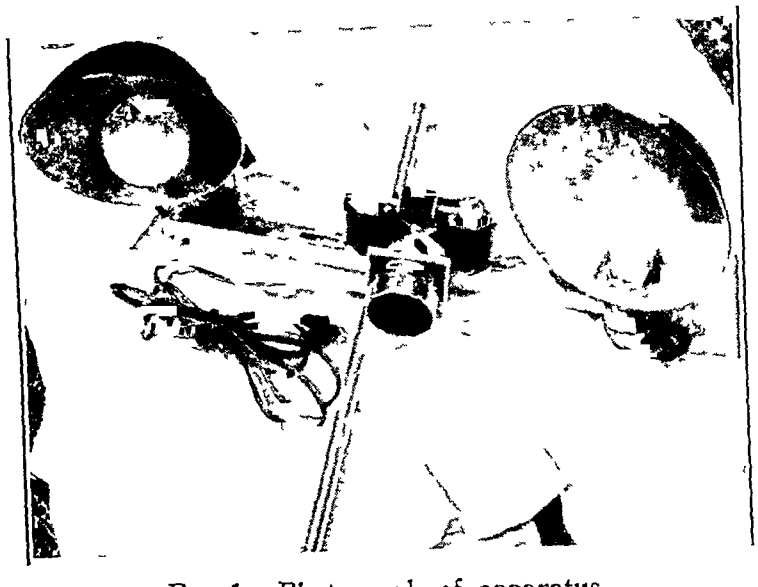


Fig 1—Photograph of apparatus

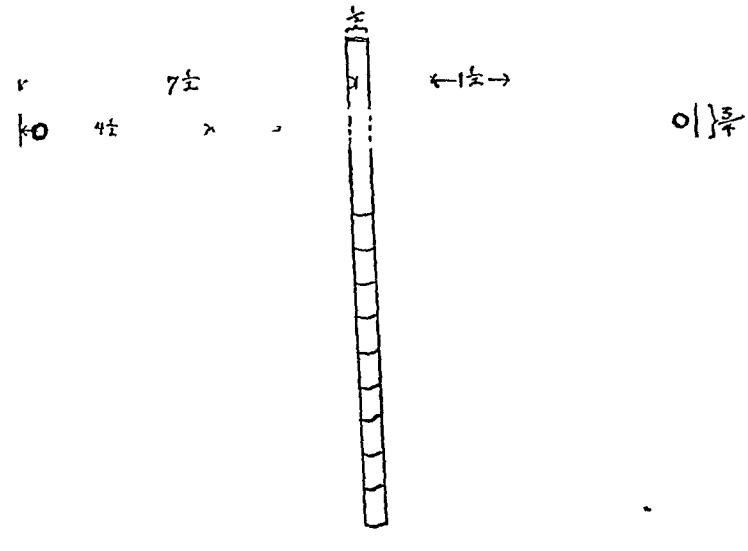


Fig 2—Diagram of apparatus Measurements shown are given in inches, as are calibrations on the focusing rod

The following figures will serve as a basis for calculating exposure data Once the proper setting for the individual apparatus has been determined, the settings may be left constant and pictures snapped at will

Lens opening	f 6
Time of exposure	1/25 second
Distance from lens to subject	10 inches
Camera (number 3 Portra® lens)	focused at 3½ feet (106 cm)
Size of field	5½ by 8 inches (14 by 20 3 cm)

131 Fulton Avenue

with no evidence of degeneration in the sensory nerves of the corium, as is evidenced by the fact that the site of an aberrant zoster lesion removed forty days later showed no such change

In this study no attempt was made to distinguish between symptomatic and idiopathic zoster However, there is no reason to believe



Fig 5—*A*, a section taken from the scar of a zoster lesion of two months' duration A large nerve bundle entering the corium from below and bifurcating shows only a few large nerve fibers and fragments of relics, × 1,000 *B*, a section taken from the scar of a thoracic zoster lesion of ten months' duration with persistent pain, longitudinal section of a nerve bundle in the middle portion of the corium A few fibers are well visualized



Fig 6—Normal skin near a brachial zoster eruption of seventeen days' duration A longitudinal section of a nerve bundle in the middle of the corium running along an artery shows only two nerve fibers In other areas of the same section nerve bundles with normal fibers were seen × 1,000

that the degeneration of the sensory nerves of the skin would differ in these two types

Virus elementary bodies and characteristic nuclear inclusion bodies are present in the very early zoster vesicle Although the virus has never been demonstrated in the affected ganglion, one may assume that it is present there also The virus seems to be neurotropic as well as

Archives of Dermatology and Syphilology

VOLUME 60 NOVEMBER 1949—PART I NUMBER 5

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HISTOLOGIC CHANGES IN SENSORY NERVES OF THE SKIN IN HERPES ZOSTER

MICHAEL H EBERT, M D
CHICAGO

THE MASTERLY postmortem studies of Head and Campbell,[1] nearly half a century ago, left little doubt that herpes zoster is associated with a severe inflammatory reaction in the sensory ganglion which supplies the sensory nerves to the area of the skin involved by the eruption Subsequent work has supported these observations However, Wohlwill[2] in 1924 showed that occasionally the inflammatory reaction might be in some other portion of the sensory tract than the ganglion Death of a ganglion cell is followed by degeneration of its peripheral axon Using the Marchi method of demonstrating myelin degeneration, Head and Campbell, as well as Wohlwill, found evidence of degeneration of peripheral sensory nerve fibers in the sensory nerve trunks ten to twelve days after onset of herpes zoster In one or two instances, some degeneration was reported by them to have taken place in the nerves of the skin, but no details are available

The present study is an attempt to demonstrate histologic changes in the nerves of the skin in herpes zoster, the time of their appearance, their extent and their location In attempting any study of the nerves of the skin, one is struck by the limitations of present knowledge These limitations were eloquently expressed by Pautrier[3] in his introductory address at the Strasbourg Reunion of 1935, when he opened a seminar on the normal and pathologic anatomy and physiology of the nerves of the skin Pautrier pointed out that most of the work of anatomists and experimentalists has been done on lower animals He emphasized that the main handicap is one of technic Silver impregnation methods are laborious and uncertain even in the hands of the most skilled

Read at the Sixty-Eighth Annual Meeting of the American Dermatological Association, Inc, San Diego, Calif, April 28, 1948

From the Department of Dermatology, the University of Illinois College of Medicine, and from the Bernard Fantus Out-Patient Clinic, the Cook County Hospital

1 Head, H, and Campbell, A W Brain **23** 353-523, 1900
2 Wohlwill, F Ztschr f d ges Neurol u Psychiat **89** 171-212, 1924
3 Pautrier, L M Bull Soc franç de dermat et syph **42** 1064-1069, 1935

disease may represent a syndrome resulting from any process causing inflammation of the spinal ganglion Others accept experimental evidence as valid proof of virus causation and regard the elementary bodies demonstrable in herpes zoster vesicles as representing the specific virus of the disease Proof that a virus causes the disease is not as readily demonstrated for herpes zoster as for herpes simplex

There is evidence of a latent state of the virus Through an interplay of circumstances—a "trigger" mechanism—the virus is awakened from a condition of dormancy In support of this theory may be cited the occurrence of zoster after sunburn, after administration of arsenical compounds and after trivial injury to the skin, following which the skin is intact

Herpes zoster provides an admirable example of a pure neurogenous mechanism in causation of cutaneous lesions There is supportive experimental evidence of this contention and, more recently, additional clinical evidence Armstrong attributed macular and urticarial lesions among Air Force personnel to mechanical irritation caused by gas bubbles in the posterior horn cells of the spinal cord

Degeneration of sensory nerve fibers after herpes zoster apparently has no clinical significance I should like to discuss this sequela but with a broader visualization Perhaps there has been too much concentration on pathologic changes of the active disease process, with neglect of the stages occurring previously and afterward In this connection I am reminded of the term "living" pathology, so well dramatized by the late John Deaver

I have always been intrigued by the corneal microscope, an admirable means of studying "living" pathology It furnishes evidence that a region or organ never, or almost never, becomes normal after pathologic involvement I refer to the "ghost" blood vessels remaining permanently in the cornea after interstitial keratitis and the changes seen by means of the slit lamp after inflammation of the anterior uveal tract I can mention demonstration of Treponema pallidum in the scar of a chancre and the histologic changes persisting at the healed site These sequelae are believed to be concerned in chancre redux

An admirable example of the sequela of a cutaneous disease is shown in the work of Madden, who demonstrated that psoriasis is present histologically after gross lesions have disappeared He thought that this represented cellular memory Perhaps we should be more concerned with the study of cellular memory and with histologic investigation at the site of retrogressed lesions of cutaneous diseases, such as lichen planus and lupus erythematosus

The opinion has recently been expressed that one may predict the type of cutaneous disease persons may get from their pattern of personality To this theory one may add the possibility, as studies of cellular memory and of sequelae of cutaneous diseases accumulate, that one may see in the microscopic mirror of what is grossly "normal" skin the ghost of past diseases and the shadows of future ones

DR MICHAEL H EBERT, Chicago I realize that this paper is not the type the lends itself well to a general discussion I appreciate all the kind things that Dr Klauder has said It seems evident that if there is destruction of some of the sensory nerve fibers in the scars of former zoster lesions there should also be a change in sensation I have made some examinations along this line and have found that there is a pronounced decrease or entire disappearance of sensation to light touch, pain and temperature in old scars of this type I was very eager to find a person with a case of leprosy with anesthetic areas whom I might use as a control for the findings I have recorded Unfortunately I was not able to find such a person

ever, Ranson and Davenport[6] showed experimentally that in the cat the sympathetic fibers in a sensory nerve bundle are relatively few While terminal axons are impregnated erratically with the method I used, the larger nerve bundles which enter the corium with an artery or vein and divide and subdivide with the blood vessels are well visualized In no instance were all the nerve bundles affected The best controls for the staining process were the unaffected nerve bundles in the same section Any supposed degeneration of nerve fibers was followed through many sections before conclusions were reached Many control specimens were taken from normal skin, nevi and skin from lesions of other types

Biopsy specimens were examined from 15 patients with herpes zoster All but 1 of these patients were male Their ages ranged from 17 to 78 The site of the eruption was thoracic in 12 instances

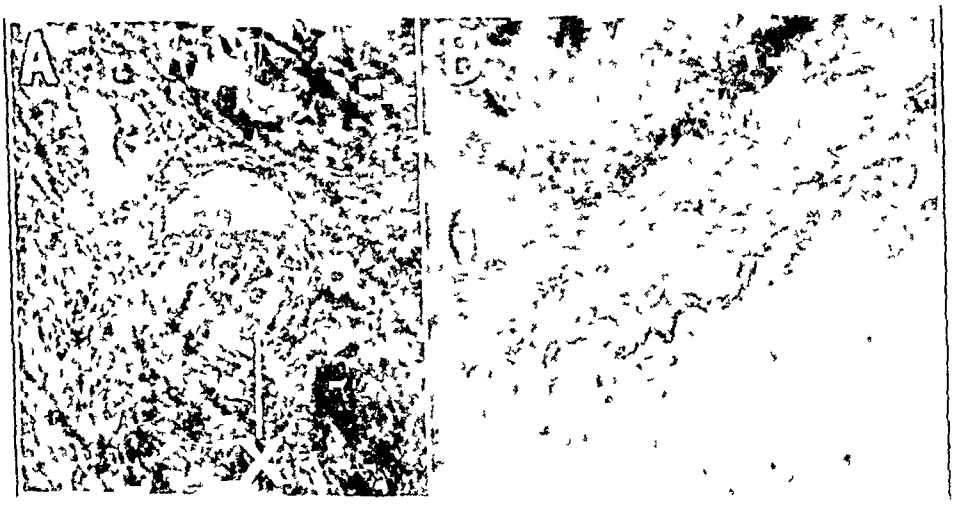


Fig 2—*A*, cross section of the nerve bundle shown in figure 1*A* The four dots at *X* are cross sections of four very fine nerve fibers The large and medium-sized fibers are sinuous and visualized as small arcs even at this magnification, × 1,000 *B*, terminal axons on the floor of a zoster vesicle of five days' duration Two very fine fibers run roughly parallel and are applied by spindle-shaped enlargements to the epidermal cells, × 1,000

There were 1 femoral and 1 brachial zoster In 1 instance the site of an aberrant vesicle was removed forty days after the appearance of a zoster generalisatus Material from 3 cases was discarded because the silver impregnation was unsatisfactory Thus the specimens in 12 cases were adequate for study

In 5 cases the vesicle was removed at periods ranging from five to thirteen days after the appearance of the eruption Among the specimens obtained in these cases was a severe gangrenous zoster removed on the eleventh day No evidence of nerve degeneration was found in any of them A vesicle was removed on the fourteenth day from a man of 69 (fig 3) and from a man of 40 (fig 4) There

6 Ranson S W, and Davenport, H K Am J Anat **48** 331-351, 1931

screw driver or pliers The test samples were spotted on a piece of elastoplast,® of about 3 by 4 inches (7 6 by 10 cm) Over 350 shoes were torn apart, these included all styles, brands and types of construction found in infants', children's, women's and men's footwear

A wide variety of materials, adhesives and dyes was found in the dissected footwear The number and types of fillers alone were impressive adhesives and cork, asphalt and cork, red, black and white sponge rubber resin and cork, plastic and sawdust and also various kinds of felts, plant fibers and leather The adhesive materials were rubber, asphalt, tar or synthetic substances Some of them had decomposed into a coarse yellow powder Over the weight-bearing portion of the sole, the filler had often become thin, or even had disappeared Fissuring and cracking of the insole was consistently observed in shoes that had been worn any length of time Often the fillers had oozed up through the cracks, staining the inside of the shoes Where the insole had fissured, it was black and brittle, apparently carbonized by the nature of the adhesive material or filler Coated fabrics or papers were cracked, the coating was peeling off, revealing two, or sometimes three to four, layers of different coating substances Patients often complained that their socks and feet stuck to the insides of their shoes Sometimes the coated insole had come loose or had worn through, with the result that the foot stuck to the filler It was amazing to observe what decomposing, sticky, tacky, filthy, sweat-soaked materials these patients, even babies and children, had laced around their feet Commonly the feet were stained by the chemical flux from the distintegrating footwear No wonder that the incidence of pedal dermatitis is so great Have dermatologists been so busy studying fungi and trying fungicides that they have overlooked the fundamentals of foot hygiene and the kinds of materials used in the construction of modern shoes?

IRRITANTS AND SENSITIZERS IN FOOTWEAR

On the basis of initial location and distribution, 160 cases of dermatitis arising from footwear were investigated and classified, in three groups group 1, dermatitis of the feet, group 2, dermatitis of the feet and hands, and group 3, generalized dermatitis

Shoe materials producing positive reactions to patch tests are listed in table 1, which also shows that certain types of materials predominated in causing these reactions in the three groups of cases

Reactions to Patch Tests with Shoe Materials—A lament frequently heard among dermatologists is that of the shortcomings of the patch test on the arm Most footwear, especially infants', children's and men's, occludes the foot as the conventional patch test adhesive plaster occludes the skin on the arm Shoes patch test the skin of the

of the nerve fiber occurs Maximow and Bloom[7] stated that the axis-cylinder breaks into irregular fragments on the third or fourth day and that in eight to ten days all that remains are scattered accumulations of fine granules

In this study, when the vesicle site was removed fourteen or more days after the appearance of the eruption, some of the nerve bundles in the middle and deeper parts of the corium were found to have much less than the normal number of nerve fibers This condition was believed to be the result of wallerian degeneration following the death of the ganglion cells All the bundles were not affected, and all the fibers in any one bundle had not disappeared This observation explains the retention of the histamine flare in the cases in which there was a test for it Evidently many of the ganglion cells regain their functional integrity

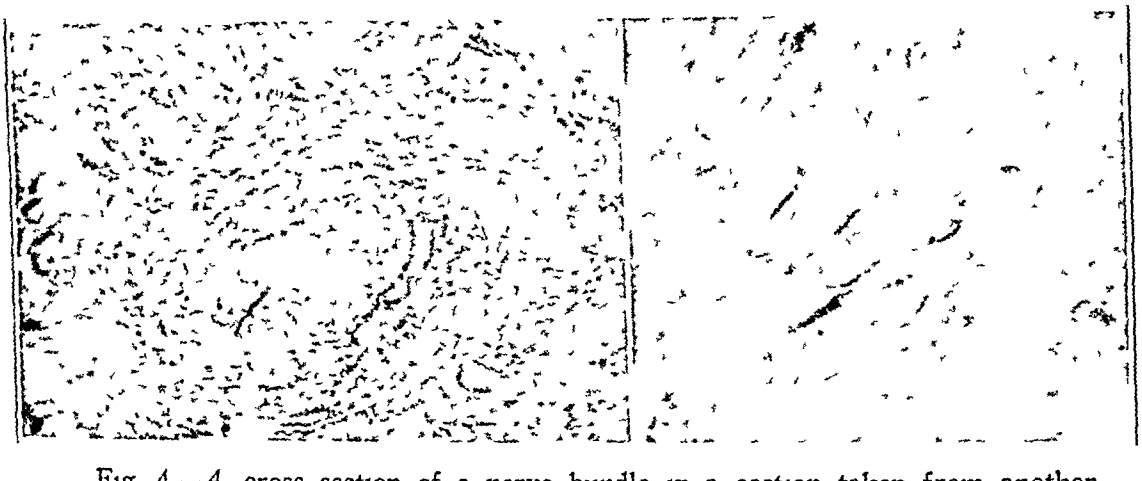


Fig 4—*A*, cross section of a nerve bundle in a section taken from another zoster lesion of fourteen days' duration The bundle is in the upper third of the corium beneath a shallow ulcer In this section only one fiber is well visualized, × 1,000 *B*, bias section of a nerve bundle in the middle of the corium The number of well stained nerve fibers is diminished more than 50 per cent at fourteen days, × 1,000

The appearance of wallerian degeneration in peripheral nerve fibers cannot be timed exactly with reference to the appearance of the cutaneous lesions New lesions continue to appear for several days, and the exact date of appearance of the lesion removed and studied could not be determined However, with this margin of error, one can safely say that the death of the ganglion cells took place at the time of the appearance of the zoster eruption or a day or two later

Wallerian degeneration occurs not only at the site of the lesion but also in the normal skin near the lesions This observation is evidence that wallerian degeneration may occur without the production of zoster vesicles On the other hand, zoster lesions may appear

7 Maximow, A A A Text Book of Histology, completed and edited by W Bloom Philadelphia, W B Saunders Company, 1930, p 304

which contains both sweat and sebaceous glands, covers, for the most part, bony and tendinous structures They permit little, if any, cushioning effect between the shoe and the skin The nails and tendinous and bony prominences wear through the socks and shoe lining, bringing the skin into direct contact with the adhesive and reenforcing materials in the shoe (fig 1) Factors of friction and rubbing constantly interplay between the foot and the shoe, with intermittent or sustained pressure favoring closer apposition Too tight a shoe can embarrass the circulation of the foot, this tendency being augmented by any vascular changes in later life Irritants in shoes that cause the foot to burn and swell bring the skin closer to the offending materials The duration of contact may be from twelve to sixteen hours, daily or intermittently for months or years, under all extreme conditions of temperature,



Fig 1—Samples removed from shoes worn by J P To the left is the right sock lining, and beneath the tip of this is the asphalt toe box To the right are the left sock lining and toe box The patient wore out the right shoe first Notice the holes in the canvas sock lining, their location corresponding to that of the five toes As the linings were worn through, the first and second toes came into direct contact with asphalt Observe how the asphalt has penetrated the lining Sock linings which have been worn through, with the result that the toes impinge on adhesive substances and toe boxes, have been consistently observed

humidity, barometric pressure and psychic disturbances Mishaps such as getting the shoes wet now and then—perhaps by spilling water in them, as children do and letting them dry on the feet expose the skin to additional extractants in footwear A wet skin, subject to mechanical friction, pressure and tension is ideal soil on which irritants work their havoc

The reactions in tests with shoe materials and with adhesive tape are compared in table 2 Commonly, at the time the patches were removed, no reaction was present An exposure to air for from ten to

dermatotropic What is the portal of entry for the zoster virus? Is it the skin, the gastrointestinal tract or the respiratory tract, or is it latent? By what route does the virus reach the sensory ganglion and the skin? Is it by the blood stream, by the lymphatics or along the sensory nerve? Does the virus multiply simultaneously in the ganglion and in the skin? If not, where does it multiply primarily? These and many other similar questions cannot be answered in the present state of knowledge and probably await the discovery of a susceptible experimental animal or new technics

SUMMARY

A silver impregnation method was used successfully to visualize the nerve bundles of the skin in 12 cases of herpes zoster

No change in the nerve bundles of the skin was demonstrable until fourteen days after the appearance of the zoster eruption

The sites of zoster lesions removed from fourteen days to a year after the appearance of the eruption showed a pronounced diminution in the number of nerve fibers in some of the bundles of the lower and middle portions of the corium

Apparently normal skin near the zoster lesions showed a similar disappearance of some of the nerve fibers

This reduction in the number of nerve fibers is an irreversible process

Zoster lesions may occur without any degeneration of the sensory nerve fibers in zoster generalisatus.

CONCLUSIONS

Death of ganglionic neurons results in wallerian degeneration of the corresponding sensory nerve fibers in the skin at the site of the zoster eruption and in the nearby normal skin

Death of the ganglion cell occurs at the time of the first appearance of the eruption or shortly thereafter

Degeneration of sensory nerve fibers may occur in areas of skin where no vesicles have appeared, and, on the other hand, the vesicles of a generalized zoster may occur with no subsequent evidence of sensory nerve degeneration

ABSTRACT OF DISCUSSION

Dr. Joseph V. Klauder, Philadelphia It is a privilege to discuss a paper pertaining to a virus disease of the skin by an author who is an authority on such diseases Indeed, it is an added privilege to discuss a study that required the investigative skill that this one did

Since I am not qualified to discuss methods of cutaneous staining, I will not select this phase

Is herpes zoster caused by a virus? The opinion has been stated by some that it has been conclusively shown that zoster is caused by a virus and that the

ing also appeared Where the cellophane® disk had shielded the skin there was no reaction, but at the periphery of the disk, especially where it was creased and a vent was produced, spots of bright erythema stood out, overshadowing even the existing reaction to adhesive tape Footwear containing fillers and adhesive substances massively patch tests the foot The appearance of reactions to patch tests after removal of the adhesive patch with the filler contactant from the footwear has an exact counterpart in the onset of signs and symptoms on the foot on removal of the shoes at night A pathognomonic sign of footwear dermatitis is the nocturnal appearance of vesicles associated with intense itching and burning The widespread incidence of irritation from adhesive plaster has a parallel in the widespread incidence of dermatitis



Fig 2 (M L) —Dermatitis on the feet, together with the footwear causing it In the lower left hand corner are samples of lining spotted on a piece of elastoplast®

pedis, because adhesive plaster and adhesive materials used in shoes are chemically and physically similar

On numerous occasions, patients were tested to the ingredients of elastoplast® Negative reactions proved puzzling Finally, tests were made with the bloomed surface of the granulated synthetic rubber Sufficient reactions were obtained to classify the antioxidant or accelerator used in the manufacture of the synthetic rubber in elastoplast® as a primary irritant No doubt the same chemicals were present in the fillers and in the samples of adhesive materials from the footwear

A positive reaction to uncoated leather always led to disclosure of an adhesive substance or a filler that produced more intense reactions,

PRIMARY IRRITANTS AND SENSITIZERS USED IN FABRICATION OF FOOTWEAR

L EDWARD GAUL, M D
AND
G B UNDERWOOD, M D
EVANSVILLE, IND

SQUEAKING shoes are today seldom encountered Not long ago they were familiar, new shoes always squeak, but taking the honors were old shoes that had been wet and then dried out The squeak was removed from footwear by radical changes in their manufacture Materials were introduced which heretofore had never touched the human foot Tennis shoes made their appearance about fifty years ago In 1910 shoe cements came into use A few years later, mineral spirits were found to be good solvents for shoe adhesives and polishes When these solvents are placed on the skin and covered, either in a patch test or by footwear, they are primary irritants and sensitizers The financial setbacks of the shoe industry in 1919 sent manufacturers scurrying for cheaper materials Various bonded, laminated, coated and impregnated fabrics or papers were introduced Many synthetic materials are now in favor Modern footwear has become a chemical labyrinth, containing, not a few hundred chemicals, but thousands [1]

Patients with dermatitis pedis, or those whose dermatitis first appeared on the feet, were asked to bring in all their shoes, whether the right or the left ones depending on which foot was more severely involved Care was taken to test every shoe as well as all the different materials The shoes were lined up as nearly as possible in the order in which they had been purchased Diligent efforts were made to pick out the footwear associated with the onset or with an exacerbation of the dermatitis Valuable information was obtained in the cases of infants and young children in which the parents had saved all the shoes For many of these patients, the mother was able to pick out the shoe connected with the onset and those associated with exacerbations Before any shoe was tested, permission was always obtained The location of the dermatitis on the foot was the clue for selecting specimens The shoes were dissected by means of a scalpel, scissors, a

1 Personal communication from Stacy-Adams Company

her feet felt hot, sticky and wet That night, when she took off her shoes, the feet were red and swollen and itched severely The next morning the tops of the toes and feet were broken out, and scattered over the back of the hands and between the fingers were myriads of little water blisters The swelling of the feet persisted, so that she was unable to get her shoes on—an unrecognized blessing On the trip home she wore a pair of cloth slippers Each time the black oxfords were worn, the feet and hands broke out Figure 3 shows the presenting dermatitis on the feet, with the shoes causing it The reactions to patch tests of the lining of the tongue and vamp, a blue-coated fabric, persisted for three months The testing site itched whenever the patient was tired or felt too warm, and the itching was especially pronounced at retiring time This case also illustrates an everyday observation Patients cutting away their shoes so as to



Fig 3 (E E)—Dermatitis of the dorsal portions of the feet, with the shoes connected with the disease The samples taken from the shoe are shown spotted on a piece of elastoplast®

get them on unwittingly eliminate the cause of their dermatitis A foot so edematous that the shoe cannot be put on is, for the time being, spared further insults from the irritants in the shoe

Case 5—K B, a white female child 15 months old, had a twelve hour contact with shoes before the onset of a generalized dermatitis She was the youngest of six children The mother had saved a pair of shoes that had been worn several months by the child's older sister The shoes were 2 years old The evening these shoes were removed the feet were bright red, swollen and covered with pinpoint-sized vesicles The shoes sharply outlined the extent of the eruption The baby was fretful and kept clawing her feet The same evening, the hands broke out, and by the next morning a generalized, patchy dermatitis was present The family

foot with the materials used in their construction under almost ideal circumstances because anatomically the foot presents the merging of specialized tissues

The soles have a thick epidermal covering, punctured by innumerable sweat pores The latter may communicate with the epidermal lymph space or be true orifices of the sweat ducts If the sweat pore communicates with the intercellular lymph spaces of the epidermis, an entrance is provided for volatile, fat-soluble and water-soluble irritants Specialized nerve endings abound in these areas Sweating is continuous on the soles and palms Psychic or physical stimulation may bathe the foot in sweat Shoes made of moisture-repellent materials, coated leather, coated paper, fabrics and adhesives, result in the foot's

TABLE 1—*Shoe Materials Associated with Dermatitis*

Shoe Materials	Acting as Primary Irritants, Group 1	Acting as Sensitizers * Group 2	Acting as Sensitizers * Group 3
Fabric and rubber toe box	6	3	1
Felt and asphalt toe box	9	10	2
Leather cemented toe box	2		
Rubber braid	1		
Black shoe polish	1		
Leather insole (asphalt filler)	3	8	1
Leather insole (plastic filler)	1		
Leather insole (rubber filler)		1	
Coated lining (paper, cloth, leather)	3	14	16
Coated heel pad	2		
Rubber lining	2	7	1
Fabric insole (rubber filler)	1		1
Cemented lining (cloth, leather)	10	14	11
Sponge rubber (fillers, arch pads)	23		1
Rubber cement		2	
Rubber welt		1	
Felt			2
Number of Cases	64	60	36

* Asphalt is also a photosensitizer Evidence in 3 cases suggested that asphalt in footwear produced a light sensitization dermatitis on the face and hands In 2 cases evidence was presented that rubber, too, may contain photosensitizing chemicals

soaking not only in its own secretions but also in the sweat extractants from the shoe The bridging film of sweat connects the epidermal covering of the foot with the materials in the footwear Socks and stockings, especially if made of nonabsorbent fabrics like nylon and rayon, afford little protection During the warm weather, women commonly wear no hose at all Socks are frequently worn through in the toes or heels House slippers often are worn without socks The skin of the interdigital webs is thin, delicate and designed for movement, like the skin covering the eyelids The webs of the fourth and fifth toes rest directly over the free lateral margin of the insole, being exposed to volatile chemicals and dust from the shoe fillers and toe box In some shoes that have been opened the filler has been almost completely pulverized The skin of the dorsal surface

slippers Every evening after wearing them her feet felt hot and would burn, sweat and itch Soon the patient could not wear these shoes for more than half a day Symptoms on the feet usually were accompanied by similar symptoms on the hands Early in December she started to get ready for the holidays A prospective son-in-law was to be a house guest Things had to be at their best While we were getting her history this remark was noted, "If things around the house don't go as they should, I get all wrought up, the sweat runs from my hands and feet" A week before Christmas, after an "especially trying day,"



Fig 5 (F D)—Showing the severity of the generalized dermatitis The shoe causing the dermatitis is to the right and the homemade cloth slippers to the left The latter, together with the all-cotton pajamas and cotton gloves, protect the entire skin except for the head When the skin is covered and immobilized as much as possible, the symptoms are effectively controlled Weeks were required for the lichenification of the soles and palms to involute

she took off the suede shoes and noted that her hose were soaked with perspiration The feet and hands began to itch, and then soon broke out and wept Several remedies were tried During the night—she described this night as the worst she had ever spent and one which she would never forget—a generalized dermatitis appeared A photograph taken eleven days after protection had been

twenty minutes seemed a necessary complement An example of a severe reaction appeared in the following case

CASE 1—M L purchased tan canvas shoes to wear in the garden They were worn intermittently for one month One evening the left big toe began to itch Masses of water blisters appeared By morning the feet showed a brilliant erythema, with vesicles and weeping The swelling prevented the patient from wearing shoes The dermatitis, after the patient had received two months of treatment for a fungous infection, is shown in figure 2, with the canvas shoes The shoes had not been worn since the onset of the dermatitis The sites of reactions to patch testing took one month to heal, leukoderma having persisted for three months at the time of writing When the inner cloth lining was pulled from the canvas upper, it was noted that the cement in some places was tacky, but for the most part had crystallized into a coarse powder

TABLE 2—*Comparison of Reactions to Patch Tests with Shoe Material and with Adhesive Plaster*

Number of cases	Group 1 64		Group 2 60		Group 3 36	
	Shoe Material	Adhesive Plaster	Shoe Material	Adhesive Plaster	Shoe Material	Adhesive Plaster
Reactions to patch tests						
Acute reactions						
Erythema, 1-2 days	27	38	12	41	1	16
Erythema, 2-7 days	31	21	21	19	6	20
Erythema, vesicles, 1 7 days	6	5	27		29	
Chronic reactions						
Negative	38	43	45	41	20	26
Erythema and scaling						
1 2 weeks			7	8	9	5
2 3 weeks	9	7	5	11	2	4
3 4 weeks	11	5			2	1
1 2 months	5	3	2		2	
2 3 months	1	6	1		1	

The reactions to patch tests with sponge rubber fillers and arch pads proved of special interest Consistently, when the patch was removed no reaction was present Gradually, a brilliant erythema developed around the sample of filler, to be followed by a reaction appearing where the sponge rubber contacted the skin After we had observed the development of many of these reactions, it seemed plausible to us that a volatile chemical, highly toxic to the cutaneous blood vessels or vasodilating nerves, was present in the filler With some of the fillers, the freshly cut surface produced the most intense reaction Does heat, moisture and pressure on fillers in footwear drive this chemical out?

The reactions to adhesive plaster closely parelleled the reactions to fillers and adhesive materials used in shoes Around the periphery of the adhesive patch, especially at the margins that had rolled, a brilliant erythema was commonly observed When the patch was removed, no reaction was disclosed until after a period of exposure to air As the reaction developed, symptoms of intense itching and burn-

cements to these materials probably made them reactive Delmonte[8] listed five different types of cements used in the shoe industry, these types are, no doubt, the basis for the many different formulas of manufacturers The reactions from sponge rubber fillers and pads are doubtless due to the presence of antioxidants and accelerators[9] An intriguing question is that concerning the degree of volatility of these materials Coatings on leather and fabric consist of shellacs, lacquers, caseins, plastics and various resins[10] Bonnevie and Marcussen[11] studied 80 cases of rubber dermatitis They concluded that the sensitizing substances in European rubber are volatile, being most active at high tem-

TABLE 3.—*Data on Patch Tests From Six Tests in Unselected Cases*

	Shoe Polishes *		Cements and Adhesives †			Leather Linings and Trims	
Brand	Primary Irritant	Smear on Filter Paper, Aged 3 Weeks	Brand	Primary Irritant	Smear on Filter Paper, Aged 3 Weeks	Materials	Reactions
						Coated Leathers	
1	Yes	—	1	Yes	+++	Beige	—
2	Yes	+	2	Yes	—	Yellow	—
3	Yes	+	3	Yes	+	Brick	++
4	No	+	4	Yes	+	Mauve	+
5	No	++++	5	Yes	+++	Tan	—
6	No	++	6	Yes	++	Blue	+++
						Linings	
7	Yes	+++++	7	Yes	+	White	—
8	Yes	++++	8	Yes	+	Rose	—
9	Yes	+++++	9	Yes	—	Green	—
10	Yes	+++++	10	Yes	+++++	Blue print	—
11	Yes	+++	11	Yes	+	Gray	—
12	Yes	++	12	Yes	+	Black	—
13	Yes	++++	13	Yes	+++	Beige	—
14	Yes	+++	14	Yes	++	White	—
15	Yes	—	15	No	++++++	Blue	—
16	Yes	+++				Leather insoles	—
17	Yes	++				Rubber braid	+++
18	No	—					
19	Yes	—					
20	Yes	—					
21	Yes	—					

* The primary irritant is doubtless the solvent Of interest are the positive reactions to the dried polishes These polishes, used on perforated shoes or on sandals, can induce a dermatitis

† Three cements, after aging for about six months, had a white bloom around the free surface Patch tests with the bloomed surface were positive in 10 unselected cases

peratures The chemicals liberated by rubber as bloom are sulfur, selenium, antioxidants, accelerators, oils and waxes They are more soluble in hot than in cold rubber and are used in proportions greater

8 Delmonte, J Technology of Adhesives, New York, Reinhold Publishing Corporation, 1947

9 Davis, C C, and Blake, J T Chemistry and Technology of Rubber, American Chemical Society Monograph Series, no 74, New York, Reinhold Publishing Corporation, 1937

10 Courtesy of Bernard Appel, M D

11 Bonnevie, P, and Marcussen, P V Rubber Products as a Widespread Cause of Eczema, Acta dermat-venereol **35** 163, 1944

suggesting that the leather had become activated or was a poor barrier for irritants Consulting the literature, we found that the following shoe materials have produced dermatitis pedis inner soles,[2] shoe polish,[3] leather inner lining,[4] leather,[5] canvas,[6] fabrikoid®,[5c] cotton stocking,[5c] tennis shoe,[3b] brown dye,[3b] felt,[3b] and tape [3b] The manner in which primary irritants and sensitizers in footwear contact the foot is illustrated by typical cases

REPORT OF TYPICAL CASES

Case 2—C S, in June 1947 started to wear a new pair of brown oxfords Within a week a dermatitis corresponding to a tack hole in the leather insole appeared on the right sole The hole measured about 3 mm in diameter and was filled with a black, sticky material The sock was stained The dermatitis had gradually spread to involve the distal half of the sole, between and over the toes Removal of the sole disclosed a cork-asphalt filler, which became soft and tacky when rolled between the fingers On patch test it caused erythema, vesicles and pustules

Case 3—C W, a veteran, had a dermatitis limited to the soles and toes which had undergone alternate remissions and recurrences for two years He was working six days a week, eight to twelve hours a day, in a pair of Government issue shoes The uppers were unlined leather The toe cap was reenforced with a rubber-cemented leather toe box The leather insole was discolored a grayish black The middle sole was leather, and the outer, rubber, both were sewed to a leather welt The soles were nailed through to the leather insole Around the free edge of the insole and each clinched nail were cones of grayish white powder Adhering to the under surface of the insole was a black, sticky canvas lining The filler consisted of tacky asphalt material in which cork was embedded The free surface was spotted with nodes of grayish white powder The shoes were over 2 years old The gray powder, leather insole, canvas lining, filler, toe box and rubber sole on patch testing produced erythema and vesicles which persisted for four days Was the gray powder over the filler a product of condensation or of disintegration, and had it reached the inside of the shoe around the holes made by the nails and the stitching?

Case 4—E E, a white housewife aged 59, purchased a pair of black oxfords to wear on a trip to St Louis to visit her son Traveling always made her nervous her hands and feet would perspire When she reached her son's home

2 Lord L W, and Wolfe, W D Dermatitis Due to Shoe Leather and to Shoe Polish, Arch Dermat & Syph **38** 434 (Sept) 1938

3 (*a*) Lord and Wolfe[2] (*b*) Shaw, C Dermatitis Due to Shoes, Arch Dermat & Syph **49** 191 (March) 1944

4 (*a*) Shaw[3b] (*b*) Lewis, G M Dermatitis Venenata Due to Shoe Leather Report of Two Cases, Arch Dermat & Syph **24** 597 (Oct) 1931 (*c*) Beerman H Factors Involved in Leather Dermatitis ibid **29** 671 (May) 1934

5 (*a*) Shaw[3b] (*b*) Lewis[4b] (*c*) Burgess, J F Contact Dermatitis of Feet Canad M A J **47** 27, 1942

6 Shaw[3b] Burgess[5c]

Distribution by Occupation—The question of whether or not scabies was present was the problem in the cases of the 11 babies and 18 children Attempts to find the acarus failed The majority of these patients had been treated for scabies at least once most of them several times—and when in doubt they were treated again Fifty-seven patients were housewives All the 13 veterans had been in the South Pacific, known for its high temperature and humidity In the remainder of the cases the patients were in various occupations common to this locality

History of Atopy—In group 1, only 4 patients had a personal history of atopy, with no family history Group 2 had 5 patients with a personal history and 6 with a family history Group 3 had 1 patient with a personal history but no family history Ninety per cent of the patients revealed no personal or familial predisposition to atopy

History of Dermatitis Venenata In group 1 16 patients had had dermatitis due to plants, 1, dermatitis from elastic in shorts, 1, dermatitis from elastic in a brassiere, 2, dermatitis from elastic in a girdle, 1, dermatitis from a rubber anklet, and 2, dermatitis from rubber gloves In group 2, 15 patients had had a dermatitis due to plants, 2, dermatitis from rubber garters, 2, dermatitis from rubber gloves, and 1, dermatitis from rubber in garters and girdles Group 3 had 11 patients with dermatitis due to plants and 3 with dermatitis caused by rubber in girdles and garters An incidence of dermatitis venenata due to plants in 26 per cent of the cases and of that caused by rubber products other than shoes in 9 per cent would suggest an acquired susceptibility to contactants However, the evidence favors contactant specificity

Length of Contact with Footwear Before Onset of Dermatitis Pedis (Incubation Period)—Marcussen [7] noted a short incubation period of from one to seven days in 8 cases and one of 3 weeks in 1 case In group 1 this time varied from ten hours to four months in 7 cases and its duration was unknown in 47 cases In group 2 it was one day in 1 case, three days in 1 case, four days in 1 case, one week in 5 cases, ten days in 1 case, two weeks in 4 cases, four months in 1 case and of unknown duration in 36 cases In group 3 it was two hours in 1 case, six hours in 1 case, twelve hours in 1 case, one day in 4 cases, two days in 3 cases, three days in 2 cases and of unknown length in 24 cases

Time Required for Exacerbation on Recontact With Shoe—Exacerbation occurred after recontact with the shoe causing the dermatitis in two hours in 1 case, in six hours in 1 case, in ten hours in 3 cases, in twelve hours to one week in 6 cases and after an unknown period in 52 cases in group 1 The length of time was ten hours in 1 case, twelve hours in 3 cases, one day in 1 case and unknown in 55 cases in group 2 In group 3 contact with the shoe causing the

physician advised scabietic treatment, and when there was no improvement the baby was treated again The five other children and the parents were not affected

During a period of three weeks, the dermatitis became steadily worse The feet and hands were a mass of draining pustules A search for the acarus proved futile, but in spite of this fact, the child was treated for scabies a third time After ten days, there was no improvement, and so a regimen of care and management was outlined to the mother The improvement in two weeks confirmed the diagnosis of dermatitis related to footwear The baby is shown in figure 4 with the etiologic shoe In the patch test both sides of the cemented white canvas lining produced a flare type of reaction The mass of cement is visible in the toe cap (fig 4) Since a sister had worn these shoes without any trouble,



Fig 4 (K. B)—Showing the pustulation on the feet after two weeks of care and management, together with the shoe causing it The mass of disintegrating cement is visible in the toe cap of the shoe

it was assumed that the cement had deteriorated over a period of two years, forming an irritating substance The baby was well within a month As the dermatitis cleared, this baby's disposition improved She was smiling, cooing and gaining weight

Case 6—F D, a white housewife aged 47, had had no cutaneous disorders until October 1944 A few days after she had begun wearing new black oxfords, the medial sole and dorsal surfaces of her feet broke out This eruption was treated as a fungous infection Within a week, the thenar and dorsal surfaces of the hands broke out Everything mentioned in the textbooks as being of value, including maximum roentgen irradiation, was used for treatment The dermatitis remained stubborn In October 1947 the patient purchased a pair of black suede

Systemic Symptoms and Signs (1) Symptoms (*a*) Psychic disturbances Our observations support a contention that somatopsychic factors are involved Convincing evidence was obtained in babies and young children With their feet and hands a mass of blisters or pustules, the diseased state of their skin registered itself in the central nervous system as fretfulness, irritability, fright, crying, insomnia and secondary manifestations such as loss of appetite, constipation or diarrhea and loss of weight These symptoms stood out in sharp contrast to the behavior of the well infant, eating, cooing, smiling and catching up on lost sleep Parents were alarmed about the afflicted child, worried about the other children's catching the disease and wondered whether their baby had an incurable condition Many of the adults, especially those with generalized dermatitis, showed lack of concentration, depression, excitability, irritability, apprehension and crying Some had difficulty in talking and were unable to express themselves because their thoughts were jumbled together Obtaining a history was difficult until the patients began to get well A mother unable to care for her children or a father unable to work had these extra worries to face That a somatopsychic state was present in these cases was supported by the large number of patients who proposed their own diagnosis, that their "nerves were jumpy enough to break the skin out" Sequeira and associates [13] aptly stated that the skin is the most extensive sensory organ and may be regarded as a peripheral brain

(*b*) Disturbances of temperature-regulating mechanism The majority of these patients were under care during hot weather While everybody else was feeling the heat, these patients complained of being cold and chilly Some of them were observed shivering when the room temperature was 90 F A dermatitis of the feet or hands, or both, apparently exerts a profound effect on the temperature-regulating mechanism of the body

(*c*) Psychic responses during as compared with those after dermatitis Patients, when questioned during the acute stages as to how they felt, would try by every means to get us to concentrate on their cutaneous lesions After they had recovered, the story was different They talked freely about how bad they had felt

(2) Signs (*a*) Temperature Patients with a severe dermatitis of the feet or hands, or both, and especially those with generalized dermatitis, commonly had subnormal temperatures Touching their skin disclosed it to be cold and frequently clammy A rise in the temperature usually heralded improvement

13 Sequeira, J H , Ingram, J T , and Brain, R T Diseases of the Skin, New York, The Macmillan Company, 1947, p 17

instituted (fig 5) shows the shoes associated with the dermatitis to the right and the homemade slippers on the left The sleeves and legs of the cotton pajamas are rolled up to show the dermatitis The reaction to patch testing—erythema and vesicles—with a cemented brown corded lining of the shoe persisted for six weeks with symptoms Tests with two prescriptions gave rise to a burning sensation, and so the testing materials were promptly removed Under protection of the skin, the generalized dermatitis cleared within three weeks The patient was well except for lichenification at the previous site of dermatitis on the feet and hands

These reactions to patch tests and especially their persistence were evidence of a highly toxic substance in footwear The brilliance of the erythema suggests a chemical which paralyzes the capillaries Edema was present, as were vesicles, and even minute pustules made their appearance Many of the reactions exfoliated for weeks or months In a few cases the skin showed loss of pigment An interesting side feature was the symptoms Itching predominated and was provoked by nervous fatigue, emotional sweating and warmth after retiring The signs of these reactions do much to explain the problems of treatment in dermatitis pedis Shoe materials contain a substance so toxic to the skin that weeks or months are required for recovery

RESULTS OF INQUIRIES TO SHOE MANUFACTURERS

As reactions to patch tests of various materials in footwear were obtained, letters were sent to the respective manufacturers asking for information about the coating substances, kinds of rubber fillers and types of adhesive substances used in making the particular shoe. Letters to companies manufacturing adhesive materials brought two samples and a decided reluctance to divulge their ingredients A survey of the dissected footwear and the correspondence from manufacturers or their suppliers forced us to the conclusion that materials were chosen for their physical properties, with little or no concern for their chemical properties A reason for the high incidence of dermatitis related to footwear is apparent after a study of table 3, which contains summaries of data on patch testing with different brands of shoe polish, shoe adhesive materials purchased in Evansville and materials used in the fabrication of shoes

Marcussen [7] tested the rapidity of diffusion of the accelerator used in the manufacture of European rubber (mercaptobenzothiazole) by placing pieces of rubber next to canvas in liquids of varying acidity and temperature and for varying periods A day in distilled water at room temperature made the canvas reactive In table 3 reactions in patch tests of the samples of fabric shoe linings were negative Applying various

7 Marcussen, P V Rubber Footwear as a Cause of Foot Eczema, Acta dermat.-venereol 22:531, 1942

sfactory routine was worked out When the eruption had cleared, patients were permitted to wear a pair of regular shoes If there s no recurrence, another pair was tried A recurrence was an indi- on for dissecting and patch testing the suspected shoe This routine vided patients with safe shoes, shoes they could wear again at the t symptom or sign of a recurrence

SECONDARY (AUTOSENSITIZATION) DERMATITIS

Our experiences offer evidence that when a chemical induces a lateral dermatitis, provided that there is sufficient exposure and the mical is sufficiently toxic, the cutaneous inflammation set up also tates the peripheral nerve endings to a point of summation, at which e stimuli break through by way of the central nervous system and unilateral dermatitis becomes bilateral This phenomenon has been erved consistently as the result of the injudicious application of ical chemicals to existing contact dermatitis, and a physical agent, h as cold quartz, also has produced it Lord and Wolfe [2] reported ase in which the eruption on the hands followed the cycle of the ption on the feet When the shoes causing the dermatitis were ioved, the hands and feet remained well This observation has been timely confirmed in our cases The hands clear up, not from the ing of alleged fungi on the feet but from the removal of the foot- ar causing the disorder

Primary Location on Feet Initiating Secondary Dermatitis on nds It is interesting that the primary lesion on the feet tended be in the same relative site as the primary sympathetic lesion on hands (table 6) In group 2 the soles and the dorsal portions he hands were involved in 1 case, the soles and the palms in 19 cases, dorsal portions of the feet and the palms in 2 cases, the entire face of both the feet and the hands in 21 cases and the entire sur- e of the toe or toes and of the finger or fingers in 2 cases The iphery of the sole or palms appeared to be a sharp dividing line e tendency for like tissues to be affected proved remarkable

Sequence of Appearance of Secondary Dermatitis on Hands—In cases, in the first attack, the entire surfaces of the feet and the hands re simultaneously involved In 3 cases, the feet were involved two eks before the appearance of lesions on the hands In 2 cases there l been remissions and exacerbations for five years before, after an ack on the feet, the hands became involved In 1 case there had n remissions and exacerbations for two years, in another, for eight nths, before the hands were involved In 1 case the left foot had n involved for two weeks, and then suddenly all of both hands re affected, two weeks later, the right foot was involved In another

than their ratio of solubility in cold rubber Therefore, it is inevitable that they tend to crystallize or otherwise separate (volatilize?) from rubber on cooling[9] Minerals frost out of some rubber more rapidly in warm, humid weather All the shoes dissected by us contained adhesives and fillers Footwear is subject to the extremes of environmental temperature and humidity and sudden changes from room to body temperature and humidity when worn

CLINICAL OBSERVATIONS

Month of Onset In the Evansville area, summer weather may appear during the last part of April and extend to October The five summer months accounted for 71 cases, whereas the remaining seven months of the year accounted for only 28 cases The month of onset was unknown in those cases in which there had been remissions and

TABLE 4—*Distribution by Age and Sex*

Decade	Group 1		Group 2		Group 3	
	Male Patients	Female Patients	Male Patients	Female Patients	Male Patients	Female Patients
First	3	2	2	8	3	7
Second	6	3	3	3		1
Third	6	5	6	8	3	1
Fourth	1	3	10	5	1	8
Fifth	4	3	5	3		5
Sixth	5	7	2	1	1	4
Seventh		5	3		1	1
Eighth	1	8				
Ninth		1	1			
Tenth	1					

exacerbations for years, especially in those in group 2 The high number of cases during the summer, especially during the hot spells, may be explained on the basis of more profuse sweating of the feet or greater volatilization, blooming or frosting of chemicals from fillers, caused by the environmental temperature and humidity Some people perspire freely during hot weather, noting little, if any, sweating of the soles; but in cold weather their soles and palms are likely to perspire freely. These people are often seen with attacks of acute dermatitis pedis following the first cold weather of the season

Distribution by Age and Sex The tendency of people in the earlier decades to be affected is shown in table 4 Emotional sweating of the palms and soles accompanies the prepuberal and postpuberal decades In over 57 per cent of these cases the patients were female Men's footwear was the more occlusive to the foot, but women's footwear, dictated by changing styles, colors and materials, offered the greatest range of exposure to irritating contactants, favored by the fashion of not wearing hose No decades were exempt from dermatitis due to footwear

Trying to trace this attack disclosed the following facts On Thanksgiving Day she had attended a local football game The home team was fighting hard She became excited The sweat dripped from her hands, her feet, too, were soaked At about 5 p m the palms were itching, and by 6 30 p m the soles were itching and burning Sometime during the night the attack arrived The appearance of the soles caught our attention The distal third was not involved, and the picture resembled the photograph of recalcitrant pustular dermatitis of the palms and soles in the textbook by Andrews [14] The shoes the patient had worn to the football game contained a purple-coated fabric insole lining, the size of which corresponded to the area of dermatitis on her soles (fig 7) Patch tests with the insoles established the cause of this attack, initiated by an emotional upset which induced sweating of the soles and palms The sweat had formed a



Fig 6 (N K)—Showing a recurrence caused by wearing the shoes to the right The two shoes on the left were the footwear associated with the onset of a previous generalized dermatitis The all-leather sandal is shown between the legs

bridge between her soles and the insole lining, which contained an irritating chemical The exacerbations following bridge games are explainable on the same basis She stated, "If I am winning, all is well, but if I am losing I get excited, my palms and soles sweat" The insoles which had caused the dermatitis were removed, and white cloth was substituted

Case 8—H K, a white housewife aged 34, is another example of a patient for whom emotional sweating induced dermatitis She was seen Nov 14, 1947, for a vesicular eczematization of the dorsa of the feet and an erythroderma of the

14 Andrews, G C Diseases of the Skin for Practitioners and Students, ed 3, Philadelphia, W B Saunders Company, 1946, p 263, fig 208

dermatitis induced an attack in ten minutes in 1 case, in two hours in 1 case, in three hours in 1 case, in six hours in 1 case and in one day in 1 case, the period required was unknown in 31 cases

Initial Locations of Dermatitis Due to Footwear Table 5 lists the initial locations of dermatitis caused by footwear Twenty patients had unilateral involvement We obtained an explanation for the choice of sites in these cases by noting whether the patients were right or left footed and, particularly, whether there was anything remarkable about their gait These peculiarities produced different degrees of wearing, and the degree of wearing seemed to have some relation to the dermatitis, that is, the shoe with the lining worn out first and the insoles fissured was usually on the foot unilaterally involved The observation that lining seams frequently determine the location suggests that there is a volatile irritant in the adhesive substances used in the shoe A geometric pattern of the dermatitis was an indication to us to search all the footwear for lining, seams and/or trim which might conform to this pattern It is apparent from an examination of table 5 that no part of the foot is spared in dermatitis associated with footwear

TABLE 5—*Initial Locations of Dermatitis Due to Footwear*

	Group 1	Group 2	Group 3
Dorsal portions of toes	11		
Dorsal portions of toes and of feet	14	15	19
Entire surfaces of feet	5	21	17
Entire surface of left foot	2		
Entire surface of right foot	2		
Entire surfaces of toes	6	2	
Soles	8	22	
Right sole	2		
Left sole	1		
Dorsal portions of left toes	9		
Dorsal portions of right toes	4		

Symptoms of Dermatitis Due to Footwear All patients presented itching, which was observed to be of all degrees of severity, as the most characteristic symptom Unforgettable sights were the babies rubbing their feet together, wildly clawing at them and, in some instances, even biting them Profuse sweating was the second most characteristic symptom Often it preceded the itching, and it is probable that it may prove to be the first warning of the presence of irritants in shoes Feet were observed actually dripping perspiration The third commonest finding was burning and swelling, and in 45 cases weeping was noted These symptoms are a reliable guide in the differential diagnosis of dermatitis of the feet Severe pedal symptoms point to footwear as the cause of disease, as was noted also by Niles,[12] Lord and Wolfe,[2] Burgess,[5c] Shaw [3b] and Lewis [4b]

12 Niles, H D Dermatitis Due to Shoe Leather, J A M A **110** 363 (Jan 29) 1938

Attacks of dermatitis pedis due to emotional sweating were observed in the following patients E H, after attending her son's wedding, M M, on going to the dentist, W Z, on attending a basketball game, and D P, after obtaining the leading part in a floor show The cases of these patients demonstrate the fact that emotional states inducing profuse sweating of the soles can initiate attacks of dermatitis by the formation of a bridge of sweat between the skin of the foot and the irritant materials in footwear

FAILURE OF MODERN FOOTWEAR TO MEET THE HYGIENIC NEEDS OF THE FOOT

All footwear dissected revealed materials which were moisture repellent Droplets of sweat have been seen covering coated heel linings Papers, fabrics and leathers were sealed with substances resistant to moisture Leather insoles were covered with coated heel pads or coated heel and arch pads The fillers sealed the under surface of leather insoles This method of shoe fabrication prevents the evaporation of sweat, allowing the insole to become an "extractor or condensor" for water-soluble and fat-soluble irritants present in the fillers Sweating from the soles and palms is a continuous and an essential function Under the influence of environmental temperature and humidity, physical exertion and/or psychic activity—fear, joy, anxiety and mental work sweating increases, often to the point of profuseness Infants' feet sweat, with this function increasing during childhood, reaching a maximum at puberty and then tending to decline with increasing age Sweating was observed, in varying degrees, in every case The preponderance of cases, in groups 1, 2 and 3, occurred in the earlier decades (see table 4)

Since sweating of the soles is a normal body function, provisions must be made in footwear to permit rapid absorption and evaporation of perspiration Leathers tanned by older methods,[15] uncoated and unpolished, readily absorbed moisture and were sufficiently porous to permit rapid evaporation, with consequent transference away from the foot of the absorbed moisture Stelwagon[16] in 1916 stated that the sole was a rare site for ringworm infection The introduction of the use of cements and other moisture-repellent materials in the manufac-

15 The Romance of Leather, New York, Tanners' Council of America McLaughlin, G D, and Theis, E R Chemistry of Leather Manufacture, American Chemical Society Monograph Series, no 10, New York, Reinhold Publishing Corporation, 1946

16 Stelwagon, H W Treatise on Diseases of the Skin for the Use of Advanced Students and Practitioners, ed 8, Philadelphia, W B Saunders Company, 1916, p 1164

(*b*) Color of the skin In a severe dermatitis of the feet or hands, a pallor was frequently noted If the dermatitis involved the feet and hands, or if it was generalized, a light olive color was commonly noted in the uninvolved skin

(*c*) Lymphangitis with adenopathy In group 1, 1 patient had an attack involving the left leg, and 1 patient had two attacks involving the right leg and one, the left leg In group 2, 9 patients had one or more attacks involving the lower or upper extremity

(*d*) Laboratory data A remarkably consistent finding was that the skin presented severe symptoms and signs and yet that the integrity

TABLE 6—*Signs, Behavior and Secondary Manifestations of Dermatitis Due to Footwear*

Initial Signs On Feet	Number of Cases	Behavior: First Attack	Behavior: Recurrent Attacks	Secondary Manifestations	
Group 1—Dermatitis on feet					
Erythema and edema	1				
Symmetric lividity	2				
Vesicular eczematization	34	32	2		
Pustular eczematization	6	5	1		
Lichenified eczematization	20	20			
Dry eczematization	1	1			
Group 2—Dermatitis of feet and hands					
Vesicular eczematization	10		10	Vesicles on hands	10
Pustular eczematization	41	31	10	Vesicles on hands	23
				Pustules on hands	18
Dry eczematization	9	9		Dry eczematization	9
Group 3—Dermatitis on feet, generalizing by way of the hands					
Pustular eczematization	27	27		Generalized Signs	
				Vesicles	12
				Pustules	2
				Atopic lesions	7
				Psoriasiform lesions	4
				Urticaria	2
Vesicular eczematization	5	5		Vesicles	5
Lichenified eczematization	2	2		Patchy lichenification	2
Nummular eczematization	2	2		Patchy nummulation	2

of the body as a whole was unaffected With the exception of consistently low hemoglobin readings (Haden-Hauser) and red blood cell counts tending to range below 4,000,000, all laboratory tests were within normal limits In only 3 cases was there albumin (a trace to 1 plus), which disappeared as the dermatitis cleared

Signs, Behavior and Secondary Manifestations The problem that confronted us in this study was finding safe shoes for the patients to wear During the summer the children were asked to go barefoot In the fall some of them were seen with recurrences caused by wearing their shoes Footwear is as much a part of modern living as is other clothing A woman cannot go shopping or a man work in a factory unless shoes are worn Various makeshifts, such as homemade cloth slippers sandals or sewed moccasins, were resorted to Many of the patients purchased handmade, untreated leather sandals like those shown in figure 6 As experience was gained in handling these cases, a highly

impregnated felts Heel counters are leather or bonded papers Liberal amounts of adhesives secure the linings to the shoe uppers The insoles are treated leather, impregnated fabrics and coated cloth or paper Heel pads are usually a coated paper Insole materials are cemented to the bottom fillers of the shoes Thus, the feet are encased in a moisture-repellent environment

2 Water-proofed materials in contact with the feet cause the skin to become sticky, especially in hot weather Imbibition of cutaneous secretions by the horny layer and possibly also the rete, because the upper third of the sweat glands is patent, promotes absorption of allergens by the pedal skin [21] Renshaw [22] demonstrated that vesicant vapors penetrated much easier through a water-saturated epidermis than through a dry skin A layer of wet filter paper did not interfere with penetration These data suggest that thin socks and hose, when wet, would not prevent the absorption of allergens in footwear

3 Factors 1 and 2 assume greater significance when it is pointed out that sweating is continuous on the palms and soles Diverse mechanisms—such as environmental changes, constitutional types and psychic and emotional stimuli—affect the degree of wetting of the feet An example is a patient who had worn intermittently for six months a strap type green pump While fishing she got her feet wet A dermatitis, demarcated by the shoe straps, appeared the same evening When factors 1 and 2 are linked up with 3, the varied clinical manifestations of allergic contact dermatitis from shoes can be pieced together The tendency for attacks to occur in hot, humid weather is readily apparent

4 The fourth factor is concerned with the role of tension and pressure in causing the cutaneous penetration of allergens Shoes are held on the feet by straps and laces, usually with the skin under tension The sole is a weight-bearing area of skin These additional factors need evaluation

The coatings on sock linings and the adhesives in footwear suggest the presence of resins or resinification of these substances by aging Resins are known to have a high sensitizing index An example of a severe dermatitis from a laminated sock lining appears in the following case

CASE 9.—O W, a white housewife aged 38, had had recurrent dermatitis on the feet every spring for six years The latest attack had appeared during the first part of May 1949 The distribution corresponded to the tongue of her shoes A topical remedy was applied and the feet wrapped in cotton gauze Adhesive

21 Rothman, S Personal communication to the authors

22 Renshaw, B Observations on the Role of Water in the Susceptibility of the Human Skin to Injury by Vesicant Vapor, J Invest Dermat 9 75, 1947

case, the left foot was involved for two weeks, and then the right foot was, two weeks later, the hands were involved The sequence was unknown in 32 cases Marcussen [7] noted a concurrent dermatitis on the hands in 6 of his 11 cases

Sequence of the Secondary Dermatitis in Group 3 As in group 2, the tendency held true in group 3 for the primary lesion on the foot to be reproduced in the generalized lesion In 12 cases signs appeared on the feet, and then the hands, after which there was sudden generalization In 8 cases there had been signs on the feet for from one week to nine months, and then there was generalizing by way of the hands In 1 case there had been remissions and exacerbations of the lesions on the feet for three years before, suddenly, there was an eruption on the hands followed by generalization In another case there had been remissions and exacerbations of the signs on the feet for fifteen years A week after an exacerbation of the pedal lesions, the hands broke out, and a week later there was a generalization In another case there had been signs on the feet for three weeks before the hands broke out, and a week later there was generalization The sequence was unknown in 13 cases Shaw [3b] and Marcussen [7] each reported 1 case of generalized dermatitis due to footwear

EMOTIONAL SWEATING INDUCING ATTACKS OF DERMATITIS PEDIS

Gathering data on the role of emotional sweating in dermatitis pedis proved the most interesting phase of this investigation

REPORTS OF TYPICAL CASES

CASE 7—N K., a white housewife aged 22, was observed in February 1947 for a generalized dermatitis, psoriasiform pustulation with alopecia, of six months' duration The eruption had first appeared on the feet after the wearing of white platform (red sponge rubber filler) slippers Under a regimen of protection, the patient was well in one month No exacerbations occurred while she wore the leather sandals shown between her feet in figure 6 The shoes associated with the dermatitis are shown to the left The shoes to the right had been worn for six hours before suddenly there was an eruption on the feet and hands A return to wearing the sandals brought about a prompt involution In June 1947 the patient obtained two pair of shoes which were made without the use of cement During the summer the shoes were worn only on special occasions The patient felt safer in the leather sandals From July to November, on six different occasions, she was seen with a mild recurrence She traced these attacks to playing bridge and thought they were due to proximity with the other players' shoes

On November 28 she had a severe attack It seemed that the previous mild recurrences had joined together to produce an explosive outburst Deep-seated pustules massed the palms and soles Was this to be a case of recalcitrant pustular dermatitis? At the first symptoms and signs of trouble, however, she had donned the cotton pajamas, gloves, socks and sandals Improvement was rapid

dichromate as the commonest offender Robins [26] described 12 cases of allergic dermatitis from shoes, in many of these cases a generalized dermatitis developed Downing [27] recorded the case of a physician who was spared a sympathectomy by discovering that shoe cement produced the trouble Sulzberger [28] expressed the belief that eczematous eruptions of the hands can occur as secondary manifestations to eczematous processes on the feet, even when the latter are not of fungous origin, for example, they may occur secondary to an eczematous contact dermatitis of the feet due to eczematogenous allergens in footwear The

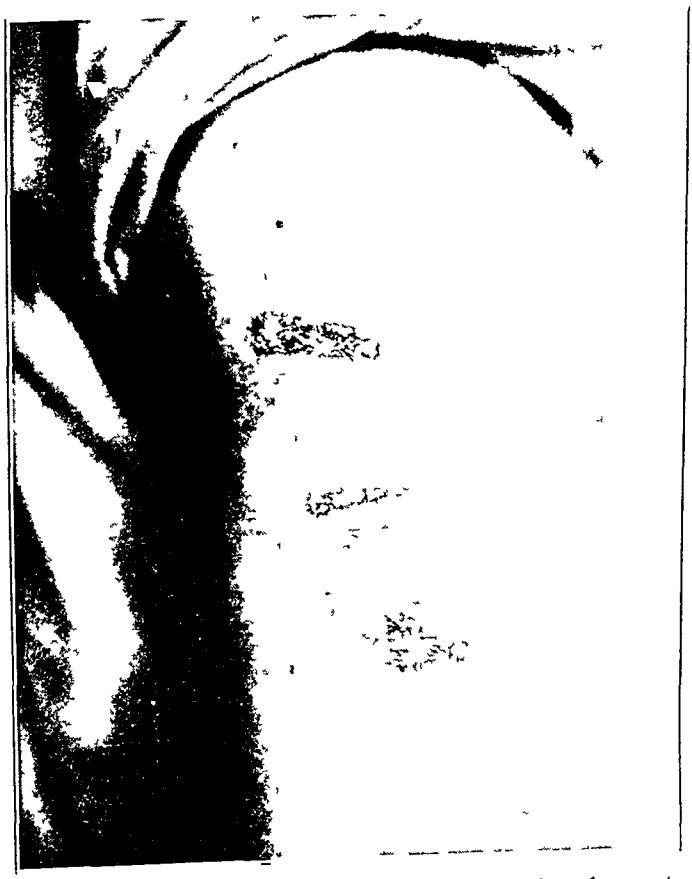


Fig 9—Bullous reactions to patch tests with the heel and toe straps of shoes shown in figure 8

cases in groups 1 and 2 add confirmation to this observation As will be noted in table 1, heels and soles of footwear as sources of allergens were considered unlikely because of the remoteness of the contact

26 Robins, A Allergic Dermatitis from Footwear, South African M J **17** 345, 1943

27 Downing, J G Trauma of the Skin Due to Wartime Activities, New England J Med **227** 539, 1942

28 Sulzberger, M B Yearbook of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc, 1949, p 14

thighs, the flexor surfaces of the arms, the neck, the face and the eyelids of three weeks' duration The eruption cleared in eight days On November 24 she appeared with an exacerbation having a similar distribution and brought with her a pair of black slippers These had been worn to church the day before She now recalled that the same shoes had been worn to church immediately before her first attack A two hour contact with the shoes had induced a dermatitis Patch tests with the blue-coated fabric insole and a gray rubber upper lining produced erythema and vesicles, the reaction persisting for two months with symptoms The second attack took over a month to involute. This observation has been made repeatedly It supports the conclusion that recurrent attacks of dermatitis induced by the same irritant become increasingly severe, requiring longer and longer periods for involution In spite of these attacks, this patient did not believe her shoes were responsible She wore them

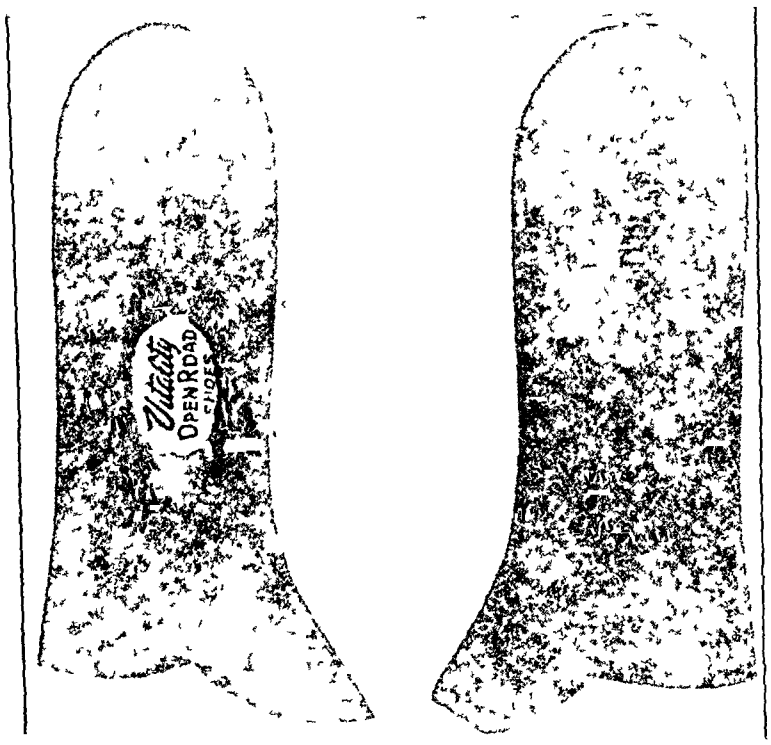


Fig 7 (N K)—Showing the purple-coated insole linings which were taken from the shoes worn to the football game These linings demarcated the pustular reaction on the soles

to a dance on New Year's Eve No attack occurred On Sunday the shoes were worn to church Shortly after the service started, her feet began to itch She slipped her shoes off and put them on again only to get to the car On Monday morning the eruption on the feet was sharply demarcated by the contour of the upper rubber lining of the shoe The soles were not involved By removing the shoes the patient had prevented a third generalized attack The insole, too, contained an irritant Attending church always brought on emotional tension, the patient's palms and soles would sweat profusely When she was asked to describe how she felt in church, her eyes brightened, her arms flexed and, with her hands clenched, she said, "I tighten up all over" Six days after the eruption on the feet reoccurred the site of the reaction in the patch test for rubber flared up and the right ear canal itched and wept Three years before, the patient had had a dermatitis of the auditory canal due to a rubber ear-adapter of a hearing aid

TREATMENT OF SYPHILIS WITH PENICILLIN INJECTION IN OIL AND WAX U S P

Analysis of One Hundred and Fifty-Three Cases

JOHN E RAUSCHKOLB, M D
AND
HAROLD N COLE, M D
With the Collaboration of Burt Held, M D, Milton H Gustafson, M D, Jack H Bowen, M D, and Manly Utterback, M D
CLEVELAND

AFTER the original report, in 1943, by Mahoney, Arnold and Harris,[1] on the treatment of syphilis with penicillin, it soon became apparent that the necessity of administering penicillin solution at frequent intervals often presented difficult problems in treatment In 1944 Romansky and Rittman [2] described a method of preparing a suspension of penicillin calcium in a mixture of white wax U S P and peanut oil (penicillin injection in oil and wax U S P) Intramuscular administration of this penicillin, peanut oil and white wax suspension at twenty-four hour intervals gave results as satisfactory as those obtained with multiple injections of penicillin in aqueous solution

From Feb 7 to Oct 19, 1946, 160 patients with primary and secondary syphilis, and 15 patients with early latent syphilis, a total series of 175, were treated by us with penicillin injection in oil and wax All these patients were hospitalized in the Cleveland City Hospital and received identical schedules of therapy, consisting of 600 000 units of penicillin administered intramuscularly once a day for eight days, for a total dose of 4,800,000 units This series consisted of 79 patients with primary syphilis, 81 with secondary and 15 with early latent syphilis In the series, 160 were men, 36 white and 124 Negro, and 15 were women, 4 white and 11 Negro

Read at the Sixty-Seventh Annual Meeting of the American Dermatological Association, Inc, Murray Bay, Quebec Canada, June 2, 1947

From the Department of Dermatology and Syphilology, Western Reserve University, and the Cleveland City Hospital, H N Cole, M D, director

The work described in this paper was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Western Reserve University, and under a grant-in-aid from the National Institute of Health, United States Public Health Service

1 Mahoney, J F, Arnold, R C, and Harris, A Penicillin Treatment of Early Syphilis A Preliminary Report, Ven Dis Inform **24** 355-357 (Dec) 1943

2 Romansky, J J, and Rittman, G E A Method of Prolonging the Action of Penicillin, Science **100** 196-198 (Sept 1) 1944

ture of footwear coincided with a phenomenal incidence of dermatophytosis Lewis and Hopper [17] stated that moisture is one of the factors thought to be predisposing toward fungous infection of the toes, and they went on to say that fungi may remain dormant for some time under natural or artificial conditions of drying, being capable of revival with the addition of moisture Hopkins [18] expressed the belief that in fungous, and also in most pyogenic, infections, moisture is an essentially predisposing factor These diseases do not occur in those who go barefoot, and the persistence of the infection is probably due to moist conditions maintained under the air-tight shoes in hot weather Results of experiments in which sandals permitting free evaporation of foot perspiration were worn allowed Nickerson, Irving and Mehmert [19] to report that dermatitis pedis could be practically removed as a cause for serious medical concern by the wearing of sandals It is true not only that modern footwear is made from irritating and sensitizing materials, but also that these materials leather, coated fabrics and papers—are moisture repellent, which characteristic predisposes the feet to contact eczematization and secondary mycotic and pyogenic infections

HOW TO PROVIDE AMERICANS WITH SAFE FOOTWEAR

A need has been expressed [20] for a Council on Dermatologic Hygiene and Therapeutics An urgent duty of this council would be an appraisal of the hygienic needs of the foot and evaluation of materials used in the manufacture of footwear with reference to their irritating properties If a need were found to eliminate certain materials, the council would be in a position to provide manufacturers with this information Footwear meeting the hygienic requirements of the feet and fabricated from safe materials should contain the seal of this council so that the public would be able to purchase shoes which conformed to certain standards

COMMENT

Four factors condition the high incidence of dermatitis from footwear 1 Sock linings of shoes consist of variously colored coated leather, canvas and a wide choice of bonded, impregnated, natural or synthetic materials Toe boxes are laminated substances, such as asphalt-

17 Lewis, G M, and Hopper, M E An introduction to Medical Mycology, Chicago, The Year Book Publishers, Inc, 1939, p 7

18 Hopkins, J D Personal communication to the authors

19 Nickerson, W J, Irving, L, and Mehmert, H E Sandals and Hygiene and Infections of the Feet, Arch Dermat & Syph **52**·365 (Nov-Dec) 1945

20 Underwood, G B, and Gaul, L E Overtreatment Dermatitis in Dermatitis Venenata Due to Plants, J A M A **138** 570 (Oct 23) 1948

interrupted, and, except for a rather severe urticarial reaction in 1 Negro with secondary syphilis, no sensitivity or local reaction to treatment was observed This absence of any allergic reaction is in contrast to the incidence of such reactions in connection with similar treatment in 5 per cent of patients as observed by Romansky[3] He did not observe fever, associated with pain and induration at the site of injection, on the fifth to seventh day of treatment, as did Thomas, Landy and Cooper[4] Nineteen of our group, including 4 patients with primary, 10 with secondary and 5 with early latent syphilis, had previously received varying amounts of aqueous penicillin for either syphilis or gonorrhea These patients likewise showed no sensitivity to the penicillin, oil and wax mixture which we used

Failure to note reactions to treatment in our series may possibly be attributed to the relatively brief period of inpatient observation, since most of our patients were discharged after the short hospital stay of eleven or twelve days However, no history of reactions or abscess formation was reported subsequently by the patient, and the physicians in the outpatient department noted no such complications Admittedly, in a larger series of cases, the incidence of local or sensitivity reactions might ultimately have reached a higher percentage

SPINAL FLUID FINDINGS

Every patient in the series had a spinal fluid examination, including cell count, total protein determination, Pandy and Nonne-Apelt tests, mastic test and a Wassermann test with ascending amounts of fluid (0 1, 0 5 and 1 cc) Of the 50 patients with primary syphilis, all 10 seronegative persons had normal spinal fluid findings Four patients among the 40 with primary syphilis who were seropositive had involvement of the central nervous system, an incidence of 10 per cent For 3 of the patients, the significant abnormality was a weakly positive Wassermann reaction, and for 1 an increased cell count and a low, "paretic" type of mastic curve The last patient was admitted for study and treatment of primary syphilis three months after hospital treatment for meningococcic meningitis, no doubt the aforementioned changes were remnants of this previous inflammation

Nineteen of the 57 patients with secondary syphilis showed abnormalities of the spinal fluid, an incidence of 33 3 per cent Only 2 were women, both white In 8 of the 19 patients, the significant finding was a weakly positive Wassermann reaction Eight patients had an increased cell count as well as a positive Wassermann reaction, 1 patient had an increased total protein content and a positive Wassermann reaction, and 2 patients had only an increased cell count

3 Romansky, J J The Current Status of Calcium Penicillin in Beeswax and Peanut Oil, Am J Med **1** 395-411 (Oct) 1946

4 Thomas, E W , Landy, S , and Cooper, C Rapid Treatment of Early Syphilis with Penicillin in Beeswax and Oil, J Ven Dis Inform **28** 19-23 (Feb) 1947

plaster was used to hold the bandage in place Soon the soles became involved with a linear eruption corresponding to the strips of tape encircling the feet The initial dermatitis erupted violently, became pustular and drained profusely The allergen in the tape easily penetrated several layers of gauze to the skin, conditioned by the presence of moisture and pressure Six weeks were required for the dermatitis to involute Early in July 1949 the patient purchased the sandals shown in figure 8 While they were being worn with hose, she was aware of burning of her feet This became so severe that she removed the shoes after six hours A bullous dermatitis appeared immediately The distribution is shown in figure 8, a photograph which was taken eight days after the onset Patch tests with samples of the sock lining, a laminated material, produced a bullous



Fig 8—Demarcation of dermatitis by shoe straps, the inner lining of which was a laminated substance

reaction, as is seen in figure 9 This housewife was partially disabled for the entire summer

Many of the chemicals used in processing hides to convert them into leather may cause dermatitis, and recently various antimildew and fungicidal chemicals have been added [23] Dolce [24] reported 10 cases of dermatitis due to leather Osborne and Dolce [25] in a study of 30 cases of shoe leather dermatitis found chromic acid and potassium

23 Schwartz, L , Tulipan, L , and Peck, S M Occupational Diseases of the Skin, ed 2, Philadelphia, Lea & Febiger, 1947, pp 299

24 Dolce, F A Shoe Dermatitis Among Soldiers, Mil Surgeon **95** 505, 1944

25 Osborne and Dolce, cited by Dolce [24]

the eleventh month, 14 had a dilution of 1 16 (4 Kahn units) or more, 11 of these were last seen within six months after therapy End results for these persons are likewise undetermined at this date Twenty-one of the 57 patients with secondary syphilis had a relapse, an incidence of 36 84 per cent

Six of the 9 patients with early latent syphilis, comprising 66 per cent of the group, had relapses The other 3 continued to show positive reactions to serologic tests in a dilution of 1 6 (4 Kahn units) or more One of these 9 patients had no record of previous treatment Four patients had received 1,600,000 units of penicillin, 1, 1,600,000 units of penicillin, as well as arsenical and bismuth therapy for one month, 1, 2,400,000 units of penicillin, 2, arsenical and bismuth therapy, and 1, a single injection of penicillin as treatment for gonorrhea

TABLE 3.—*Distribution of Patients by Serologic Response to Treatment*

Stage of Disease	Serologic Reaction Negative	Serologic Reaction Positive: 1 to 8 Dilution or Less (2 Kahn Units)	Serologic Reaction Positive: 1 to 16 Dilution or More (4 Kahn Units)	Relapses or Reinfections
Primary syphilis				
Seronegative (10)	9			1
Seropositive (40)	24	2	6	8
Patients (50)				
Secondary syphilis				
Patients (57)	17	5	14	21
Early latent syphilis				
Patients (9)			3	6

In all, 36 patients of the total 116 had a relapse, showed persistence of seropositive reactions or were reinfected, an incidence of 31 03 per cent

Among the 9 patients with primary syphilis who had a relapse or became reinfected, the only seronegative person who had a relapse had it three months after treament One seropositive patient had a relapse within two months, and the last 2 in the series had a relapse in the eleventh month Of the 21 patients with secondary syphilis who had relapses, 52 38 per cent had them in the first six months Of the 6 patients with early latent syphilis who had relapses, 2 had them in the fifth and sixth months, 1, in the eighth month, and 3, in the tenth and eleventh month

The 36 patients known to date to have made unsatisfactory responses to the scheduled therapy have been identified as follows The largest group were classified as having had clinical relapses These constituted 55 5 per cent of the series, and the relapses were recognized by

SUMMARY

This report pays tribute to those patients who during their examinations remarked, "I can cure my feet by going barefoot" and the young girl from the deep South who said, "I never had trouble with my feet till I came up north to work Where I was raised, we didn't wear shoes much" Fungicides to destroy the dermatophytes have failed both in the prevention and in the treatment of dermatitis pedis To provide Americans with safe footwear is the responsibility of dermatologists

509 Hulman Building

of the group to identify the episodes as relapses or reinfections has led us to an opinion in favor of relapses Indeed, in only 1 case were there satisfied in any essential degree the criteria generally accepted for establishing the diagnosis of reinfection Some authorities would term it a case of relapse

REPORT OF A CASE

N M, a Negro, with a primary syphilitic lesion of the prepuce, was admitted for diagnosis and treatment on May 14, 1946 The serologic reaction was positive and dark field illumination revealed T pallidum He gave a history of having had a penile sore with a positive serologic reaction in April 1945, while in service in the Navy He stated that he had then received sixty injections of penicillin On May 16, 1946, diagnosis having been established, he was treated with 4,800,000 units of calcium penicillin in white wax U S P and oil for the usual eight days and was discharged to the outpatient service on May 23 Within three and one-half months, on August 29, his serologic reaction became negative This was confirmed by negative serologic reactions obtained on Nov 16, 1946, and Feb 8, 1947 On March 4, 1947 he was readmitted to the hospital with multiple primary lesions on the glans penis and on the prepuce (the site of the primary lesion in May 1946) and regional adenitis Dark field illumination revealed T pallidum on March 5 The serologic reaction was strongly positive, in a titer of 1 128, on March 5 Examination of the spinal fluid on May 1946 gave normal findings except for a weakly positive Wassermann reaction, 1 plus in 0 5 cc and 2 plus in 1 0 cc dilution The serologic reaction of the spinal fluid on March 5, 1947 was entirely negative The patient gave a history of exposure in January to a patient under treatment for syphilis in our clinic, on this admission he was treated with 4,800,000 units of crystalline penicillin G

SUMMARY AND CONCLUSION

Of the series of 116 patients with active syphilis from an initial group of 175 patients with primary and secondary syphilis, and a small group with early latent syphilis, 36, or 31 03 per cent, had a relapse or became reinfected, including 1 with primary seronegative syphilis One patient of the 36 might be considered as having reinfection, the others may be said to have had serologic relapses, persistent seropositive reactions or clinical relapses Of those who had a relapse, 20, or 55 5 per cent, were recognized as having a clinical relapse, 11, or 30 5 per cent, as being seropersistent, and 5, or 13 5 per cent, as having a sero-relapse

Daily injections of 600,000 units of penicillin in white wax and oil constitute therapy of practical value for syphilis The dose of 4,800,000 units so given permitted a relapse or reinfection rate of 31 03 per cent Supplementation of this treatment or increase in the dose may be desirable in an attempt to decrease this rate of relapse

Western Reserve University

Of the total series of 175 patients, 59, or 33 5 per cent, were lost from observation or the cases closed, and data concerning them therefore could not be included in any statistical compilation This group comprised 29 patients with primary, 24 with secondary and 6 with early latent syphilis

The remaining 116 patients formed the series with active syphilis followed and provided the statistical basis or data for this report The series considered here was composed of 50 patients with primary syphilis, all male, of whom 14 were white and 36, Negro, 57 with secondary syphilis, of whom 51 were male (10 white and 41 Negro) and 6, female (3 white and 3 Negro), and 9 patients with early latent syphilis (2 white men, 5 Negro men, 1 white woman and 1 Negro woman)

TABLE 1—*Distribution of Patients by Stage of Disease, Sex and Race*

	Men		Women		
Stage of Syphilis	Negro	White	Negro	White	Total
Primary	59	20	0	0	79
Secondary	56	13	9	3	81
Early latent	9	3	2	1	15
Total	124	36	11	4	175

TABLE 2—*Distribution of Patients with Active Syphilis*

	Men		Women		
Stage of Syphilis	Negro	White	Negro	White	Total
Primary	36	14	0	0	50
Secondary	41	10	3	3	57
Early latent	5	2	1	1	9
Total	82	26	4	4	116

In the group of 50 patients with primary syphilis, 10 were seronegative and 40 were seropositive Dark field examination revealed Treponema pallidum in 32 cases and failed to show the organisms in 16, and the results were not recorded in 2

METHOD OF TREATMENT

When a patient was admitted for diagnosis and treatment, he was invariably studied by means of careful physical examination, dark field examination of material from any open lesions, serologic tests of the blood and lumbar puncture Three days were generally occupied in assembling pertinent data, and then therapy was instituted

Treatment was given by a trained staff, consisting of the resident physicians, assisted by the department nurses Injections of 600,000 units of penicillin in oil and wax were given intramuscularly in the upper outer quadrant of the buttock, on alternate sides, for eight consecutive days In no case was treatment

It has been amply demonstrated that pretreatment abnormalities of the spinal fluid bear no relation to post-treatment abnormalities, the latter are associated with clinical and serologic relapse It would appear, therefore, that the results of pretreatment lumbar puncture are of only academic interest, and that lumbar punctures should not be performed routinely

The authors' relapse rate for primary and secondary syphilis, 18 and 36 per cent, respectively, seems rather high as compared with Thomas' rate of 9 and 14 per cent The difference is difficult to explain

Finally, the authors report only a single instance of reinfection, an evaluation which is ultraconservative, especially since 50 of their 116 patients had primary syphilis I wonder what Dr Schoch's study and analysis would be in their series of cases

This brings me to the discussion of Dr Schoch's presentation Early in our work with the "five day therapy," my associates and I became convinced that a considerable number of our "infectious relapses" were in fact reinfections This opinion was based on the accepted criteria for reinfection

Dr Schoch, engaged in a similar study of intensive therapy, came to the same conclusion and, with commendable zeal, has since been active in attempting to prove this point In spite of the formidable array of data that he has presented, Dr Schoch will probably be the first to acknowledge that thus far he has not completely proved his thesis, that verification is something to occur in the future

Most investigators in this field admit that reinfection occurs, but contend that it is rare as compared with the incidence of infectious relapse Dr Schoch, on the other hand, holds the opposite view, and in his most recent statistics presents a proportion of 60 per cent of cases of reinfection to 40 per cent of cases of relapse The entire issue hinges on intensive therapy in syphilis, and bearing directly on this problem is the acknowledged fact that together with the increasing improvement in the treatment of syphilis, a progressive increase in the number of reinfections is reported

Before the general use of arsphenamine only a few patients were cured, hence, reinfection was rare During the early use of arsphenamine with conventional arsenical therapy, more patients were cured and more cases of reinfection were reported. However, with the introduction of intensive, shortened methods of therapy with arsenicals and/or penicillin, the number of reinfections reported has mounted greatly, at least fivefold to tenfold This apparently leads to the conclusion that modern therapy does produce a greater number of cures, and, given the necessary conditions of exposure and infected source, a greater number of reinfections are to be expected

Since reinfection is predicated on the cure of syphilis, the question arises What is meant by a cure? Is a symptomatic or a serologic cure sufficient? I think not Cure, in my opinion, means, in the strict sense, a biologic cure, one in which not only every organism has been destroyed, but in which the immunization process, if it developed at all, has disappeared and not even a trace of reagin remains A cure in this sense is a restoring of the patient to his preinfected state, obviously, such a patient if infected anew should be considered as reinfected

Granted that patients given proper therapy who show a low titer (complement fixation readings of 10 or less, or a quantitative Kahn titer of 16 or less) often become seronegative, can we say that this occurs in all cases? And if it persists, can we say, then, that the infection is completely gone? Hardly

Dr Schoch, however, is content with less strict criteria, and believes that a cure, and hence a reinfection, is compatible with "a substantial amount of reagin

Two of the 9 patients with early latent syphilis had positive Wassermann reaction of the spinal fluid

There were 24 positive reactions of the spinal fluid in the series of 116 cases of active syphilis, an incidence of 20 7 per cent We plan to restudy these cases at the end of a year

Under treatment as outlined, the lesions healed promptly, in a manner comparable to that observed with arsenical therapy Reactions of lesions that had previously been positive on dark field examination invariably became negative within twenty-four hours after initial therapy Patients were discharged with lesions healed, usually the day after the eighth injection of penicillin, to be followed in the outpatient department by physical examination with regular monthly titered serologic tests of the blood

The technic used at Cleveland City Hospital is that of a centrifuged resuspension with the employment of Kline exclusion antigen and the test is read grossly [5] Titers are reported by progressive dilution from 1 1 Roughly, 4 units in the Cleveland City Hospital technic corresponds to 1 Kahn unit A titrated serologic test gives a better indication of the patient's response to treatment The direction of the titer and its rise or fall are significant

RESULTS

Among the 50 patients with primary syphilis, of the 10 persons who had been seronegative, 9 remained so Thirty-two of the 40 patients who had been seropositive were kept under observation after their initial therapy of 4,800,000 units of penicillin calcium in white wax and oil, with the following results

Twenty-four patients became seronegative, 33 per cent in the first month, 83 per cent by the end of the fifth month and all by the end of the eleventh month

Two had a dilution of 1 8 (2 Kahn units) or less when last seen, 1 in the second and 1 in the ninth month after treatment

Six had a dilution of 1 16 (4 Kahn units) or more, when last seen

The end result had not been determined at the time of writing Five of these patients were in the second month after therapy

Nine of the patients with primary syphilis, 1 of whom was seronegative and 8 seropositive, had a relapse or became reinfected This number represents 18 per cent of the group of 50

Seventeen patients with secondary syphilis became seronegative by the tenth month Five had a dilution of 1 8 (2 Kahn units) or less by

[5] Lund, H Titration of Traces of Reagin Technique of Flocculation Using Maximal Serum Proportions with Secondary Recovery of Antigen, Am J Syph Gonor & Ven Dis **26** 1-15 (Jan) 1942

Dr Romansky and Dr Koch used 300,000 units of penicillin daily for eight and ten days, respectively, while the others used 600,000 units daily for eight days The results in all these series have shown a lower failure rate than those of Dr Rauschkolb and Dr Cole

Dr Thomas reports unsatisfactory results in 14 9 per cent of the largest series available to date, one of 802 patients In a small series, of 75 patients, treated with this dose of penicillin in white wax and oil in Detroit, from March to July 1946, failure to date has occurred in 10 4 per cent, 27 6 per cent are still seropositive, and 62 per cent are seronegative

In another series, of 90 patients, treated with a special schedule of 600,000 units twice weekly for eight weeks (sixteen doses, a total of 9,600,000 in units), even more promising results were obtained, that is, 10 9 per cent were therapeutic failures (4 per cent probably having reinfections), 15 6 per cent were seropositive, and 73 5 per cent were seronegative In reporting the results of these groups, it is assumed that the proportion of patients with primary syphilis to patients with secondary and recurrent secondary syphilis is relatively uniform, otherwise, large variations in results could be expected

In general, these available reports indicate a rate of failure of 10 to 15 per cent, in contrast to Dr Rauschkolb's rate of 31 per cent However, it is a human frailty to become overenthusiastic about a new method of treatment, it may well be that further observation and experience will establish Dr Rauschkolb's and Dr Cole's figures as being the more accurate

There is argument whether 300,000 units is not as effective as 600,000 units daily, and Dr Mahoney has stated that commercial penicillin in white wax and oil as marketed is variable in potency, or at least has been until recently

I was pleased to hear Dr Rauschkolb's statement that they had practically no allergic reactions in their group Generally, in other reported series such reactions have occurred in about 5 per cent of the cases and occasionally necessitated discontinuance of penicillin treatment

I was surprised to hear of the high percentage of positive reactions of the spinal fluid in Dr Rauschkolb's series Their figures compare well with the expected incidence of 30 per cent of positive reactions of the spinal fluid in cases of early syphilis as established by the Cooperative Clinic Group

However, throughout the experience with intensive therapy of early syphilis, it has been an unexpected finding that the incidence of positive reactions of the spinal fluid has been low In the Detroit series, only 3 5 per cent of more than 1,200 spinal fluids were classified as seropositive

I have devoted practically all of my time to the discussion of delayed absorption of penicillin and have little remaining for Dr Schoch's paper However, this has been done thoroughly by Dr Chargin

Dr Schoch is to be congratulated on coining the term "ping-pong syphilis" and emphasizing its frequency after intensive treatment For the most part, I agree with his figures, his illustrative cases, which he did not have time to report, emphasize that he is conservative in classifying a case as one of reinfection rather than as one of clinical relapse I must say, however, that the rate of promiscuity in Dallas must be even higher than that in Detroit

I agree that the incidence of reinfection is much more frequent in cases of treated primary syphilis than in cases of treated secondary syphilis I suspect that with more accurate histories a duration of secondary manifestations could be determined after which reinfection does not occur, in other words, lasting immunity develops

the reappearance of cutaneous or mucocutaneous lesions In 11 patients, 30 5 per cent, the positivity of titered serologic tests persisted at its pretreatment level for extremes of three to twelve months and a median of nine months These patients are designated, for the purposes of this paper, as seropersistent It is realized that Thomas and others were inclined to view seropersistence, if the titer was low, with no great alarm, even though it might run for several months In 5 patients, or 13 5 per cent, the initial apparently satisfactory serologic response gave way to a positive serologic reaction, with higher titer These reversals are here termed serorelapses

TABLE 4.—*Distribution of Patients by Post-Treatment Month in Which Relapses and Reinfections Occurred*

Stage of Syphilis	Month 1	2	3	4	5	6	7	8	9	10	11	12	Total
Primary		1	1	1	2					2	2	.	9
Secondary		1	1		6	3	1	2	1	3	2	1	21
Early latent					1	1		1		1	2		6

TABLE 5.—*Distribution of Patients by Number of Relapses*

Stage of Syphilis	Men		Women		Total
	Negro	White	Negro	White	
Primary					
Seropersistence	1	0	0	0	1
Serorelapse	1	0	0	0	1
Clinical relapse	7	0	0	0	7
Secondary					
Seropersistence	4	1	1	1	7
Serorelapse	2	1	1	0	4
Clinical relapse	9	1	0	0	10
Early latent					
Seropersistence	2	0	0	1	3
Serorelapse	0	0	0	0	0
Clinical relapse	1	2	0	0	3
Total	27	5	2	2	36

The correlation of pretreatment serologic responses of the spinal fluid and the number of relapses was as follows No patient with primary syphilis who had a relapse or became reinfected had a positive reaction of the spinal fluid before treatment Ten of the 21 patients with secondary syphilis who had relapses had positive reactions of the spinal fluid before treatment One of the 6 with early latent syphilis who had a relapse had a positive reaction of the spinal fluid

The 36 patients, 31 03 per cent of the series with active syphilis, whose positive serologic reactions either continued to be positive or relapsed to positivity, or whose clinical symptoms indicated recurrence, are evaluated as representing relapses or reinfections Critical review

antisyphilitic agents used in the treatment of this disease. Nevertheless, the final decision will depend on the results of ten to twenty years of observation of syphilitic patients treated with penicillin, when it may be determined how many have relapsed, and how many by slow progression have arrived at the chronic, tertiary stage of the infection

This new remedy is handicapped by the "modern style" of rapid treatment, if penicillin had been discovered fifteen years ago, the methods of treatment would have been entirely different With this agent of lower toxicity, the newer approach, which seeks to eradicate this previously unpredictable organism in a short time rather than over a longer period, use of repeated minor "attacks" may be correct Nevertheless, I believe that our attitude should be one of waiting Spirochetes have been, and still may be, the downfall of many!

In the clinic of the University of Virginia, we have treated a relatively small group with penicillin in oil and white wax by giving two injections of 600,000 units each twice a week for eight weeks To date, the rate of failure is only about 10 per cent, in our shorter schedules of treatment, with sodium penicillin in aqueous solution and including all time-dose schedules, our rate of failure is nearly 30 per cent It may be concluded, then, that treatment over a longer period has a real advantage, not only in curing the patient, but possibly in keeping him under treatment long enough to allow his original contact to become noninfectious This would avoid the cases of "ping-pong" syphilis mentioned by Dr Schoch There may be, then, two real advantages in the longer course of treatment, namely, a higher rate of cure and the prevention of spread There is both laboratory and clinical evidence to suggest that a continuous high level of penicillin in the blood is not necessary in the cure of this infection

Dr Schoch's statements and conclusions with regard to reinfections are interesting, but I, like some of the other discussers, feel that the decision in the individual case may be subject to a difference of opinion It does not necessarily follow that if a treated syphilitic patient has had sexual contact with another syphilitic person he will become reinfected The figures and details of the serologic findings in these cases might be used as an argument in favor of the diagnosis of infectious relapse rather than of reinfection

DR. CHARLES R REIN, New York Dr Romansky and I have treated patients with early syphilis with penicillin in peanut oil and white wax with excellent results, our rate of relapse has been less than 5 per cent Recently we have been using crystalline penicillin G in single doses of 300,000 units per day for sixteen days, thus far our clinical and serologic results seem better than those obtained with amorphous penicillin We have experienced no technical difficulties in the administration of penicillin in the oil and white wax

It does not seem fair to classify as treatment failures those patients who did not become seronegative within the first year after therapy, it has been our experience that such patients may attain seronegativity during the second year

We believe also that it is often possible to differentiate between relapse and reinfection by carefully conducted quantitative serologic studies made at frequent intervals In the case of reinfection, the patient usually attains and maintains complete seronegativity after the development of a dark field—positive, seronegative lesion at a new site Shortly afterward, seropositive reactions develop with rapidly increasing titers It is also possible that some patients with a residual positive serologic reaction from a previous infection may have a new primary lesion at another site, in some patients a reinfection may even develop with no clinical evidence of a new primary or secondary lesion In patients who were treatment failures or who had a relapse, we noticed first a sudden increase in

ABSTRACT OF DISCUSSION ON PAPERS BY DRS RAUSCHKOLB AND COLE AND DRS SCHOCH AND ALEXANDER

DR. LOUIS CHARGIN, New York I shall discuss Dr Rauschkolb's paper first We have just heard the presentation of an excellent clinical study It furnishes important data which will help to evaluate the use of penicillin injection in oil and wax U S P in the treatment of syphilis, and I feel that such evaluation must be based largely on clinical studies

In their presentation, Dr Rauschkolb and Dr Cole have analyzed and stressed especially the negative results, I should like to spend a few minutes allotted for the discussion in analyzing the data from the standpoint of positive results On the whole, though the results in their series of 116 cases cannot be considered highly favorable, they are not entirely disappointing

Analysis of their figures shows that in 43 per cent of the cases, during an observation period of eleven months seronegativity was attained and seems likely to be maintained In 6 per cent there was a positive serologic reaction of lower titer, these reactions may be expected to disappear in a short time

Thus, in somewhat less than 50 per cent of the cases the outcome may be regarded as showing as satisfactory This number may be further improved on While 20 per cent of the patients show a positive serologic reaction in dilution of 1 16 or more, a certain number even of these—very likely only a small number—may achieve seronegativity

Then, too, of the 31 per cent recorded as having had a relapse, some may actually have been reinfected The final figure for a satisfactory outcome may therefore be somewhat higher than 50 per cent This figure may be compared with the satisfactory one of 60 per cent recorded in the cumulative report of the centers where rapid treatment is given, and where, as you know, various intensive methods of treatment including the use of 2,400,000 units of aqueous penicillin, are employed

The figure of 60 per cent just cited may now be regarded as a base line for intensive methods of therapy since they have all given almost identical long term results There is, then, a 10 per cent difference favoring rapid treatment schedules at these centers, as against methods of therapy employed by Dr Rauschkolb and Dr Cole

However, Thomas, in a similar study of 802 cases, presented figures in each of the categories that are much better than those of Dr Rauschkolb and Dr Cole His figure of satisfactory results parallels the base line of 60 per cent previously mentioned I do not know what might account for the marked difference between the results obtained by Dr Rauschkolb and Dr Cole and those of Dr Thomas

It is not unlikely, and is in fact probable, that a schedule of treatment using smaller doses of penicillin in white wax and oil over a longer period will produce superior results It is with this time-dose factor in mind that our group in New York has undertaken a study, now in full progress, in which crystalline penicillin G in doses of 300,000 units in white wax and oil is administered once a day for sixteen days, although not consecutively, since treatment is omitted on Sundays

Our results thus far in 150 cases justify an optimistic outlook I am fully in accord with Dr Rauschkolb and Dr Cole that the rather high failure rates reported in cases of secondary syphilis and in some primary cases of seropositive syphilis with various schedules of penicillin therapy make it desirable for additive and/or synergistic medication to be introduced, primary seronegative syphilis offers no problem

REINFECTION AND RELAPSE AFTER TREATMENT OF EARLY SYPHILIS WITH PENICILLIN

Analysis of One Hundred and Thirty-Seven Cases of "Infectious Failure" in a Total Series of 1,105 Cases

ARTHUR G SCHOCH, M D
AND
LEE J ALEXANDER, M D
DALLAS, TEXAS

WE use the term "infectious failure" (infectious relapse) to describe all cases in which, months or years after treatment with penicillin for early syphilis, patients exhibited dark field positive lesions morphologically typical of primary and/or secondary syphilis All other types of failures of penicillin therapy were excluded from the study During the three and one-half years prior to the time of writing, we have collected a sufficient amount of detailed data on 137 cases of infectious failure to enable us to differentiate reinfection and relapse in the majority of instances

Of the 137 cases subjected to critical, detailed collective and individual analysis, the diagnosis of reinfection was made in 80, leaving 57 in the category of relapse (table 1)

CLINICAL AND LABORATORY FACILITIES FOR COLLECTING DATA

In November 1943, at the beginning of the study of the penicillin therapy of early syphilis, as a specially trained investigating team of physicians, nurses and technicians, we were already functioning at the Dallas Syphilis and Venereal Disease Clinic For the previous three year period we had been engaged in investigating the use of rapid methods of treatment of early syphilis, namely, the ten day injection technic and the Eagle and Hogan triweekly method By November 1943, investigations to determine contacts were being carried out in a highly efficient manner [1] Quantitative serologic tests had been in use in

This study was aided by grants from the United States Public Health Service

From the Department of Dermatology and Syphilology, Southwestern Medical College, and the Dallas Syphilis and Venereal Disease Clinic

Read at the Sixty-Seventh Annual Meeting of the American Dermatological Association, Inc, Murray Bay, Quebec, Canada, June 2, 1947

1 Miss Dorothy Lee, head serologist, has been in charge of the laboratory from 1931 to the time of writing

remaining" While in the nonsyphilitic person a small amount of reagin means nothing, this can hardly be true for the person who has syphilis

Our differing viewpoints cannot be reconciled by mere statements, that will come with more precise experimental study My personal feeling is that a successful reinoculation in the presence of reagin should be considered not as a reinfection but, rather, as a superinfection, infectious relapse, reinoculation or reactivation, the term depending on the other factors present However, if one is content with the less strict interpretation of Dr Schoch—and Dr Schoch may be right—then, obviously, the occurrence of reinfection becomes relatively common According to my interpretation, some of Dr Schoch's cases would hardly conform to the stricter criteria of reinfection

To summarize While I agree with Dr Schoch in most of his contentions, I am loath to accept his opinion in the matter of reagin To discuss briefly two more points First, everyone will agree that primary syphilis is readily cured by intensive methods of therapy If so, reinfection should be commoner among patients so cured Dr Schoch's [run back] statistics are illuminating in this respect Of 80 cases of reinfection, 50 are credited to the group with primary syphilis, despite the fact that most of his patients began treatment during the secondary period of their infection Second, not enough stress is being placed on the behavior of the serologic test in differentiating infectious relapse from reinfection It is now well established that in infectious relapse there occurs a progressive upswing of the serologic titer days, and even weeks, before the appearance of the clinical lesion

Dr Loren W Shaffer, Detroit Penicillin has been used in the treatment of syphilis for nearly four years, and we still cannot be didactic as to its most effective time-dose relationship

Early in 1946, commercial penicillin was recognized as containing forms F, G, K and X Form K came to be present in increasing amounts and has been proved practically inert in the treatment of syphilis Nearly pure penicillin G became available in July 1946, and reevaluation of penicillin, starting nearly from the beginning, was necessary

Sufficient time has not elapsed to establish more than a trend toward cure However, these trends seem favorable, and it is possible that the poor results reported to date for long term studies (with an over-all failure rate of 30 to 40 per cent in cases of early syphilis) can be materially improved on Dr Mahoney's recent figures on results of soluble penicillin given at two hour intervals around the clock would seemingly establish its superiority over the three hour schedule Extremely large doses with resultant higher blood levels are unnecessary and are a waste of penicillin

The newest development has been the delayed absorption of penicillin, as exemplified in penicillin in peanut oil and white wax U S P This method has the great advantage of permitting treatment of ambulatory patients or of office management Sufficient time has not elapsed to appraise the effectiveness of this preparation with accuracy

The expressed fear of the occurrence of local foreign body reactions has not been realized It is hoped, however, that further chemical investigations will develop a penicillin which will of itself be only slowly soluble

Dr Rauschkolb has just reviewed Dr Cole's and his experience with penicillin in white wax and oil Reports are also available through Thomas, Romansky, Koch and others, and Dr Schoch has a large series on which I hope he will report

A tentative diagnosis of relapse was made if evidence of secondary syphilis was present without a new primary lesion and if, under our observation, a sudden and definite increase of serum reagin had appeared a few weeks or months prior to the development of secondary syphilis (case 2) We realize that variations must be observed, but in the majority of instances a slow, gradual rise in reagin, requiring two to six weeks, indicates reinfection, on the other hand, a sudden rise, followed by infectious secondary lesions, strongly suggests relapse

A tentative diagnosis of reinfection versus relapse was made if most of the evidence pointed to reinfection rather than to relapse but was not yet conclusive (case 3)

A tentative diagnosis of relapse versus reinfection was made if the bulk of the evidence indicated relapse rather than reinfection but collateral evidence was not yet available (case 4)

After classification, the patients were admitted for retreatment with penicillin, many on a schedule identical with that used in treating the original infection

All available facilities were concentrated on gathering contact data on persons contacted and information on each patient not already available to us In this connection, it may be added parenthetically that a taxi driver, well known to our investigating team, frequently furnished information in regard to a patient's possible and probable contacts which could not be obtained from the patient In many instances this information enabled us to bring in contacts for examination who otherwise would not have been found

Recently, we have completely reviewed all these records Collateral information concerning the patients and their contacts with regard to their families, living conditions, social life and sexual activity was furnished by Miss Pauline Whatley, chief nurse, who acquired the information not only in the clinic, but in the field as well

ANALYSIS OF DATA

The first step in the procedure was to make a definite diagnosis of either reinfection or relapse for each of the 137 patients This was done recently by a detailed review of each case record by us, first individually and then together

In our opinion, 80 cases represented definite reinfection In all but 6 instances we had complete epidemiologic data indicating that the patients had been reexposed to infectious syphilis, and there was overwhelming collateral evidence that the remaining 6 patients had had ample opportunity to reacquire syphilis, together with typical clinical evidence of reinfection (dark field–positive primary lesions) In addition, for each patient a rising reagin curve typical of that observed

I also agree that in cases of reinfection there is a satisfactory response to retreatment In fact, when there is doubt whether a case is one of reinfection or one of clinical relapse, the rate of serologic reversal after treatment offers valuable confirmation

Finally, I am glad Dr Schoch did not offer any specific crtieria for reinfection He emphasized epidermologic evidence of exposure to an infectious contact, the serologic pattern and the clinical findings Beyond this, the differentiation is a question of sound clinical judgment, unbiased by any desire beyond that for the truth

Dr Herbert S Alden, Atlanta, Georgia I shall be as brief as possible, but a short resumé of Dr Albert Heyman's experience in the treatment of syphilis and his results may be of interest He believes, as Dr Shaffer expressed here, that a dose of more than 2,000,000 units of penicillin is not of any specific value, and that it is wasting penicillin to use more

He reports that he has treated 324 patients with neurosyphilis with penicillin alone, in doses of 2,400,000 to 6,000,000 units All these patients had strongly positive reactions of the spinal fluid, most of them had no symptoms There were approximately 20 patients with dementia paralytica, 8 with optic nerve atrophy, 15 with tabes, 10 with meningitis and 50 with meningovascular neurosyphilis

Of the whole group there were approximately 15 per cent who showed serologic relapse of the spinal fluid, many of the patients continued to show only progression of symptoms Only the patients with early dementia paralytica apparently did well with penicillin It is Dr Heyman's impression that the patients with moderately severe or extremely severe dementia paralytica who did poorly with penicillin would probably have done better with fever therapy Only 5 of the 8 patients with optic nerve atrophy showed an arrested process one year after treatment, 2 of these, however, had had supplementary fever therapy He observed that 10 per cent, a small proportion, of reactions of the spinal fluid became negative within a year after treatment

Dr Heyman treated 33 patients with secondary syphilis complicated with pregnancy, none of these patients gave birth to syphilitic children, and 3 of them had induction of labor during the course of treatment He treated 84 children with congenital syphilis, and approximately 75 per cent of these children are doing well, with reversal of their serologic reactions Seroresistance is not uncommon in children over 6 months of age who are treated for syphilis

A few of Dr Heyman's patients died, but nearly all these were infants who were moribund or prematurely born, and would probably have died with arsenical and bismuth therapy He feels that penicillin therapy is the treatment of choice for syphilis in infants, for neurosyphilis and for prenatal syphilis

Most of his patients with primary and secondary syphilis have been treated with penicillin in white wax and oil, with an over-all relapse rate of 21 per cent, these results are as good, however, as those with aqueous penicillin, and he recommends its use in treatment of this disease

Dr Dudley C Smith, University, Virginia Any statement made now concerning the permanent efficacy of penicillin in the treatment of syphilis must be considered preliminary Syphilis is an infection caused by an organism which acts slowly and has a tendency to "burrow" into the hidden recesses of human tissue Past experience warns us not to become overzealous about new "specific cures"

On the basis of short time experience, penicillin takes first place in syphilotherapy when its spirochetal action and low toxicity are compared with other

amount of penicillin treatment The data indicate that reinfection occurs more frequently after treatment for primary syphilis than after treatment for secondary syphilis No similar evaluation was made in the 57 cases in which the diagnosis was that of relapse, because it is our impression that this group is an admixture of patients with possible reinfections and patients with definite relapses We believe that until a relapse can be diagnosed with the same degree of certainty as reinfection an analysis of this group would be misleading

A definite diagnosis of reinfection can be made only when a considerable amount of additional data, both subjective and objective, is available, this is usually not forthcoming even with good routine clinic practice The study of penicillin therapy made available adequate personnel in sufficient numbers to collect the additional data

Table 4 indicates that the highest rate of reinfections occurred after the first treatment schedule, namely, 300,000 units of penicillin administered in seven and a half days We know, of course, that this treatment schedule is inadequate The second schedule, 1,200,000 units of penicillin given in three and three-fourths days, is also considered inadequate for the treatment of early syphilis by the Central Statistical Unit There was a strong contrast in the incidence of reinfection between the groups treated with the two schedules, yet the observation periods were comparable Even when cases of reinfection are included with those of infectious relapse and both are regarded as representing infectious failures, as is done by the Central Statistical Unit, there remains a considerable difference in the results of the two schedules for which we have no adequate explanation

TABLE 3.—*Original Diagnosis in Cases of Reinfection*

	No of Cases
Seronegative primary syphilis	10
Seropositive primary syphilis	40
Secondary syphilis	30
Total reinfections	80

The third and fourth treatment schedules differ primarily in the length of the observation period It is of interest to note that the number of patients treated with these two schedules was practically identical and that the number of relapses was practically the same with each, but that the incidence of reinfection for the third schedule was almost twice that for the fourth, these figures correspond with the period of post-treatment observation, the period in the third schedule being twice that in the fourth

serologic titer, followed, in about one month for the majority of cases, by clinical evidence of a mucocutaneous relapse

DR HERBERT RATTNER, Chicago I wish to support the contention of Dr Schoch that reinfection in syphilis occurs much oftener than is generally realized My colleagues and I became aware of it very early in our studies with intensive treatment, and, as with Dr Schoch, our conviction was born of clinical experience We saw several cases of what was later called "ping-pong" syphilis and others in which circumstances undoubtedly indicated new infection, even though it did not fulfill the then established criteria for reinfection Without new factual data it is difficult to revise an old concept and I sympathize with Dr Schoch's attempt to do so, but clinical experience should not be disregarded completely, and clinical experience does support this concept

DR JOHN E RAUSCHKOLB, Cleveland It should be remembered that this study and similar studies are attempts to develop a method of relatively intensive and ambulatory treatment for syphilis Patients thus treated could then be cared for in the outpatient department and by the practicing physician, as a matter of fact, the method is an eight day, one injection per day schedule

We purposely approached this study conservatively, the series is small as compared with that of Dr Thomas and his associates In our study the patients were observed for eleven months, all were originally hospitalized for the initial diagnostic check-up, and their treatment was later continued in the outpatient department

Our clinical rate of relapse averaged 19 per cent, but the addition of the 12 per cent of seropersistent patients brings the total incidence of unsatisfactory results for our series to 31 per cent

DR ARTHUR G SCHOCH, Dallas, Texas I have permission from Dr Arnold and Dr Mahoney to tell you about their series of experiments on rabbits In an effort to determine whether or not reinoculation was possible in the presence of reagin, they reinoculated a series of rabbits ten days after the rabbits had received a curative dose of penicillin Residual reagin was present in all instances at the time of reinoculation They obtained a reinfection in 100 per cent of the animals, but in only 30 per cent did a second primary lesion develop at the site of reinoculation I think these experiments on rabbits are of paramount importance

During the past seven months we have made a distinct attempt to curtail reinfection by the following method We now give all uninfected contacts three injections on the same day—900,000 units of penicillin in oil and white wax, U S P, 3 cc of bismuth ethylcamphorate, intramuscularly, and 60 mg of oxophenarsine hydrochloride U S P, intravenously These patients are then examined monthly, clinically and serologically Although it is much too early to gain more than preliminary impressions, we have observed no evidence of syphilis developed in any such contact in a series of about 80 patients treated during the past seven months

still under observation at the time of this report, are showing a satisfactory reduction of reagin in the blood serum in the third, fifth, seventh and tenth months of observation, respectively, after the second course of treatment It is our offhand impression that these patients have been responding as well as, or better than, could be expected We further believe that certain persons are easier to cure of early infectious syphilis than others and that in all probability the difference in patients is inherent rather than having any reference to the strain responsible for the infection The data in table 5 substantiate this assumption

We realize that many statements made in this report are hypothetic, but we believe that all have practical value We are firm in our belief that, with adequate data, the diagnosis of reinfection can be made with a greater degree of accuracy than most medical diagnoses, particularly that of latent syphilis

TABLE 5.—*Results of Retreatment of Reinfected Patients According to Schedules Used for Original Infections*

	Number
Patient cured	21
Outcome pending	4
Lost contact with patient	3
Total	28

REPORT OF FOUR CASES

CASE 1.—*Reinfection*

J D D, a white man, was admitted to the clinic on Oct 9, 1945, with dark field-positive, seronegative primary syphilis Results of the Kolmer, Kahn, Kline and Mazzini tests on the blood were negative Examination of the spinal fluid taken on the same day showed no white blood cells and 46 mg of protein per hundred cubic centimeters, results of the Kolmer complement fixation test were negative for 1 cc and smaller amounts of fluid, and the colloidal gold curve was normal The patient was treated with penicillin in oil and wax U S P (600,000 units daily for eight consecutive days) Treatment was completed on October 16, without event except for minor serologic evidence of reagin Results of the Wassermann, Mazzini and Kline tests of the blood were then negative, but the reaction to the qualitative Kahn test was 034

On his original admission, the patient named 3 contacts (1) F B, a white woman, admitted Sept 5, 1945, with secondary syphilis, (2) J M, a white woman, seronegative and clinically well when first examined, on Oct 9, 1945, but admitted for treatment on November 14, with dark field-positive, seronegative primary syphilis, and (3) R K, a white woman, examined Oct 19, 1945, when she was clinically well and serologically negative, with negative results of dark field examination of material from the "normal cervix"

Serologic tests, done on the patient's serum in the middle of November, yielded negative reactions On December 28, he returned to the clinic with a single ulcerative lesion of a few days' duration on the left side of the coronal sulcus,

the serology laboratory for almost ten years In the serology laboratory, at least three standard tests have been subjected to quantitative analysis, at the time of this report four quantitative tests are in regular use Results have been checked daily with a separate laboratory in order to eliminate, as much as possible, normal fluctuation and technical and clerical errors

The three case workers assigned to follow up the patients were specially trained graduate nurses, whose insight into the problem in general was well above average and whose enthusiasm, after six years' work on various experimental treatment schedules for early syphilis, was still exceptional

The medical examiners had terms of service in the department varying from two to ten years Clinical and dark field examinations were not relegated to inexperienced interns, assistant residents or junior fellows

TABLE 1—*Results of Penicillin Treatment of 1,105 Patients with Early Syphilis*

	Number	Percentage
Patients with reinfections	80	7 24
Patients with relapse	57	5 16
Total "infectious failures"	137	12 40

Furthermore, the Dallas Syphilis and Venereal Disease Clinic is strategically located in Parkland Hospital (the city and county hospital), the teaching hospital for Southwestern Medical College, it is also the only clinic for the treatment of venereal diseases in Dallas county, where the population is in excess of a half million persons This feature enabled us to collect accurate data on named contacts in our own department without having to rely on findings from adjacent clinics We feel that this feature has enabled us to collect data on a much more efficient basis than we should otherwise have been able to do

METHOD OF DIAGNOSIS

When a patient presented clinical lesions after treatment with penicillin for early syphilis (infectious failure), a tentative diagnosis was noted on the patient's chart by one of us (L J A) as follows reinfection, relapse, reinfection versus relapse, or relapse versus reinfection

The diagnosis of reinfection was not originally placed on the record unless all data pertaining to a patient's contacts were already in our files For example, if a man with a second primary lesion, dark field positive, named a woman as a recent contact, and our files indicated that this woman had been treated by us four weeks previously for secondary syphilis, we had proof that the patient had had an opportunity to acquire a reinfection (case 1)

in the reagin in the serum for several months preceding the appearance of the new lesions on the scalp

CASE 3.—*Reinfection vs relapse*

B D, a Negro boy of 15, was admitted on March 21, 1945, his condition having been diagnosed as seropositive primary syphilis on the basis of a positive reaction on dark field examination of material obtained from an ulcer of approximately three weeks' duration on the tip of a redundant prepuce. Serologic tests on the blood serum yielded positive reactions with the Kolmer complement fixation test and the Kline, Kahn and Mazzini flocculation tests. The titer for the Kline test was 4 dilution units, and for the Mazzini test 8 units. Examinations indicated that the spinal fluid was normal (the Kolmer reaction was negative for 1 cc. and smaller amounts of fluid, there were 1 white blood cell per cubic millimeter and 38 mg. of protein per hundred cubic centimeters and the colloidal gold curve was normal). Treatment consisted of 1,200,000 units of penicillin, plus five injections of bismuth subsalicylate, in eight days.

Recovery was uneventful clinically, and quantitative serologic tests made at monthly intervals during April, May, June, July, August and September, with almost clocklike precision, all gave negative reactions (these included the Kolmer complement fixation test and the Kahn, Kline and Mazzini flocculation tests). The last test for which a negative reaction was obtained was made on September 21, exactly six months after the original diagnosis and the beginning of treatment. Ten days later, on October 1, the patient presented himself with a new dark field–positive lesion, associated with negative Wassermann and Kahn reactions, but doubtful reactions to the Kline and Mazzini tests. The patient was retreated in exactly the same manner as for his first infection, and during the next three months some of the four serologic tests exhibited some degree of positivity. Thereafter, results of all tests became negative, and the patient is clinically and serologically well at the time of this report.

At the time of his first admission, this patient named two contacts: (1) J T, who had been admitted to the clinic for treatment with penicillin two days previously, with dark field–positive secondary syphilis, and (2) E M T, whom we were unable to find, because she had moved away.

At the time of probable reinfection, on October 1, the patient again named J T, who in the interim had married the patient and had become and remained clinically and serologically well after treatment with penicillin. Prolonged follow-up of this contact indicated that she had remained free from further infection. The patient named another contact (L M W), but she was not located.

The second primary lesion was at a different site, the coronal sulcus, the results were doubtful in two of four serologic tests for syphilis (ten days previously the patient had been completely seronegative, as evidenced by four serologic tests). The spinal fluid, at the time of the second diagnosis, was normal. During and after the second infection, the amount of reagin in the serum increased, reaching its peak of only 2 Kline flocculation units and falling again to normal in the usual period for new infections (three months). At the time of writing, the patient has apparently been cured of the second infection on the same schedule of treatment that was administered for the first infection. He has been under observation for over a year after the supposed reinfection. The only information lacking is proof that L M W had infectious syphilis.

CASE 4.—*Relapse vs reinfection*

L F, a Negro girl of 17, was first admitted on May 24, 1945, with dark field–positive, seropositive secondary syphilis. She received 1,200,000 units of penicillin,

for patients through the incubation period and the development of the primary stage of syphilis was in each patient's file Data on hundreds of contacts observed by us established this typical curve as characteristic of new infection

After the final diagnosis of reinfection was made in 80 cases, the 57 questionable cases were relegated to the category of relapse We then subjected the 80 cases of reinfection to various types of analysis (tables 1 through 6) We wish to emphasize that of the 57 cases of relapse, an indefinite number probably were instances of reinfection, but the diagnosis of relapse was made primarily because we were unable to collect sufficient objective data to enable us to establish the diagnosis of reinfection Of the entire series of 1,105 cases, there were only 6 in which the evidence was overwhelmingly in favor of relapse (case 2 is an example)

COMMENT

The most striking observation to us was that relapse and reinfection made their appearance with almost equal incidence during the first twelve months of observation after treatment of early syphilis with

TABLE 2—*Development of Reinfection or Relapse After Treatment*

	Time in Months		
	2-12	13-26	Total
Patients with reinfection	56	24	80
Patients with relapse . .	54	3	57

penicillin During the second year of observation (the thirteenth to the twenty-sixth month) reinfection continued to make its appearance, at approximately one-half the rate during the first year of observation, whereas relapse was almost conspicuous by its absence Only 3 cases of relapse were observed in the thirteenth to the twenty-sixth month, and in none of them was there overwhelming evidence in favor of relapse (table 2)

A second point of interest was that in 50 of the 80 cases of reinfection the original treatment had been received for primary syphilis and in 30 for secondary syphilis (table 3) This relation of the incidence of primary syphilis to that of secondary syphilis is just the reverse of the relation between the all-over incidence of the two stages regularly observed in the clinic during the past ten years Approximately 40 per cent of patients reporting for diagnosis and treatment for the original infection are observed in the primary stages of the disease, and about 60 per cent in the secondary stages Without bringing up the question of reinfection or superinfection, we are of the opinion that secondary syphilis is more difficult to cure than primary syphilis with a given

The over-all incidence of reinfection in this study was 7 24 per cent, and that of infectious relapse was 5 16 per cent

The incidence of reinfection was about equal to that of infectious relapse during the first year after treatment and continued to be high during the second year

Infectious relapse occurred almost entirely during the first year after treatment and, in our experience, was rare during the second year

Reinfection was much more prevalent in patients originally treated for primary syphilis than in patients treated for secondary syphilis

A small group of patients with the diagnosis of reinfection received the same treatment for the second infection as for the first The response to retreatment was exceptionally good

CONCLUSIONS

On the basis of data collected for this study, we feel justified in drawing the following conclusions

1 Reinfection is more prevalent than infectious relapse

2 For practical purposes of differentiation, any patient who presents clinical signs of infectious syphilis one year or more after penicillin treatment for early syphilis should be regarded as having a reinfection rather than an infectious relapse

3 The treatment of reinfection is more successful than the treatment of early syphilis in general

4 Since we have made a diagnosis of reinfection in the majority of instances, we disapprove of grouping together patients with reinfection and patients with infectious relapse as representing "infectious failure"

5 The diagnosis of reinfection is relatively simple, provided adequate subjective and objective data are available We have particular reference to serologic titer curves and positive epidemiologic findings

Parkland Hospital

The fifth schedule, use of penicillin plus oxophenarsine hydrochloride U S P (mapharsen®) and a bismuth compound, with an observation period of nine months or over, yielded the lowest incidence of reinfection as well as of relapse It is of interest to compare the number of relapses in this group of patients with the number in the group treated according to the second schedule The number of patients treated was almost the same, there was considerable difference in the length of observation, but since the majority of relapses appeared to occur in the first year after treatment, it is of interest to note that there were nine times as many relapses in the group treated in three and three-fourths days as in the group treated with penicillin plus oxophenarsine hydrochloride and bismuth

The number of reinfections observed after the second schedule is almost twice that observed after treatment according to the fifth schedule Since reinfection is not largely limited, as is relapse, to the first year of

TABLE 4.—*Incidence of Reinfection or Relapse After Various Treatment Schedules*

Penicillin Administered	Number of Patients			
	Total	Reinfection	Relapse	Observation Period
300,000 units, 7½ days	212	29 (13 7%)	18	3 yr
1,200,000 units, 3¾ days	160	9 (5 6%)	9	2½ yr
1,200,000 units, plus bismuth, 7½ days	296	24 (8 1%)	15	1½ yr
4,800,000 units penicillin calcium	289	13 (4 5%)	14	9 mo
2,400,000 units, in oil and wax, 8 days plus bismuth and oxophenarsine hydrochloride, 8 days	148	5 (3 4%)	1	9 mo
Total	1,105	80	57	

observation, it seems logical that this difference in incidence of reinfection between the two schedules occurs because of the difference in length of the post-treatment observation periods, greater than two and a half years in one instance and nine months in the other

Table 5 indicates that when patients with reinfections were treated according to a schedule identical with that used for treatment of the original infection results were uniformly good Even before the beginning of the study of penicillin therapy, we reasoned that any patient who is cured in a week or ten days and who subsequently becomes reinfected with a homologous, or even heterologous, strain of spirochetes should be curable on the same treatment schedule as readily for the second infection as for the first We therefore made an effort to retreat as many patients as possible with definitely diagnosed reinfection at the time of the "infectious failure" episode according to the schedule used for the original infection Data for this small group of 25 patients, recorded in table 5, indicate a perfect result in 21 of 25 The remaining 4 patients,

repetitious to include the details here However, several points may be emphasized at this time

In regard to the general character of the process, the reported cases vary from localized and relatively fixed lesions to generalized, progressive and eruptive processes, and, in addition, other cases of this nature have been reported with evidence that they definitely were of diseases belonging to the lymphoblastoma group In most of the cases of more generalized disease, a definite eosinophilia, often of considerable degree, was exhibited, while in the localized cases this feature was lacking There was no uniformity as regards atopic diathesis in patients, although in a few of the more generalized cases there was either personal or family history of some disorder of this type

Histologically there is also a discrepancy, in that some of the cases have included a distinct involvement of the blood vessels in the form of endarteritis and perivasculitis, while in others this was not found although a reticuloendotheliosis was observed Lewis and Cormia [4] commented on this situation and Weidman [3] presented a combined etiologic and pathologic classification which takes note of this fact

The question of the relationship of eosinophilic granuloma of the skin to other disorders has received much attention Especially is this statement true in regard to a group recognized as histiocytosis, eosinophilic granuloma of bone, Hand-Schuller-Christian disease and Letterer-Siwe disease

It has been assumed that eosinophilic granuloma of the skin was not related to this group However, under the title of eosinophilic granuloma of bone, Curtis [7] reported a case in which the histologic findings in the cutaneous lesions, as well as the clinical appearance, were very similar to those reported by others in cases of eosinophilic granuloma of the skin without demonstrable bone lesions It would seem at least possible that there is more than a coincident relationship

As was previously noted, some of the cases have occurred in persons with some form of lymphoblastoma In addition, O'Leary [8] observed a case very similar to our case 1, which he suggested as an example of eosinophilic leukemia

The relation of some instances of eosinophilic granuloma of the skin to disorders of probable allergic nature, such as periarteritis nodosa and Loffler's syndrome, has been noted by Lewis and Cormia and by Weidman Buley suggested that histamine or histamine-like substances might produce an eosinophilic syndrome, which could well complicate and obscure the usual clinical and histologic picture in a variety of disease entities

7 Curtis, A C, and Cawley, E P Eosinophilic Granuloma of the Bone with Cutaneous Manifestations, Arch Dermat & Syph **55** 810-818 (June) 1947

8 O'Leary, P A Personal communication to the authors

this lesion was dark field positive At this time he named 1 contact only (R K) He was retreated with 4,800,000 units of penicillin in oil and wax, given in eight days Four serologic tests on the serum and repeated examinations of the spinal fluid gave negative results on the date of readmission His recovery was uneventful, and results of regular monthly serologic tests (Kolmer complement fixation and Kahn, Kline and Mazzini) on his blood were all negative through Feb 19, 1947, at the time of report

R K, his only contact since he was first cured, was brought back to the clinic and was found to have secondary syphilis, dark field positive, on Dec 28, 1945, the day the patient returned with a reinfection

It should be noted that the patient apparently was cured of his first infection with 4,800,000 units of penicillin in oil and wax and that, fifteen months after the second infection, observation indicates that the patient has been cured for the second time on the same schedule of treatment (We agree with Dr Evan Thomas [2] that neither persuasion nor education effects return of contacts for regular periodic observations)

CASE 2—*Relapse*

E D, a white man, was first examined in the clinic April 12, 1946 He had a sparse eruption, consisting of a few scattered papules on the trunk, very small papular lesions of the glans and four crusted lesions on the scalp Results of dark field examination of the penile lesion, repeated several times, were negative, but a positive result was obtained on examination of a crusted lesion of the scalp over the vertex Quantitative serologic tests indicated titers of 8 Kline dilution units and 16 Mazzini and Kolmer units, and the reaction to the quantitative Kahn test was strongly positive

The patient named his wife as his only contact She was examined the day after his examination and was found to have a generalized, typical eruption of secondary syphilis of four weeks' standing, a high titer and dark field-positive lesions on the vulva

The patient received 2,400,000 units of penicillin, plus 320 mg of oxophenarsine hydrochloride and five injections of bismuth subsalicylate, in eight days The patient's wife received the same type of treatment during the same week She progressed satisfactorily, became seronegative by the sixth month and is still normal at the time of this report, after eleven months of observation

The patient's post-treatment serologic titer fell steadily during the first, second, third, fourth, fifth and sixth months of observation It reached a low level of 2 flocculation Kline units, at that time the reaction to the Kolmer test was positive, the titer of the quantitative Kahn test was 16 units and the titer of the Mazzini test 4 units In the seventh month the titer of the Kahn test had increased to 32 units On January 9, five weeks later, the titer of the quantitative Kahn test was 256 units Objectively, the patient was free of any eruption on this date One month later, the titer of the quantitative Kahn test was 512 units, and the titer of the quantitative Kline test was 16 dilution units On that date the patient presented six crusted lesions on the scalp, two of which gave positive reactions on dark field examination There were no concomitant lesions of early syphilis The genitalia were normal

The patient denied having had any sexual exposure He and his wife separated at the time of their original treatment, and both denied further contact

The lesions on the patient's scalp at the time of relapse were unusual morphologically, dark field positive and identical in appearance with those presented on the first admission, which were also dark field positive There was an increase

2 Thomas, E Personal communication to the authors

appear enlarged on palpation or percussion, and there was no superficial adenopathy beyond that readily explainable on the basis of the manifestly pustular cutaneous lesions to be described

The distal portions of both the upper and the lower extremities showed decided pitting edema and were the seat of numerous pea-sized to small coin-sized vesicles and vesicopustules In addition, there were numerous scattered pea-

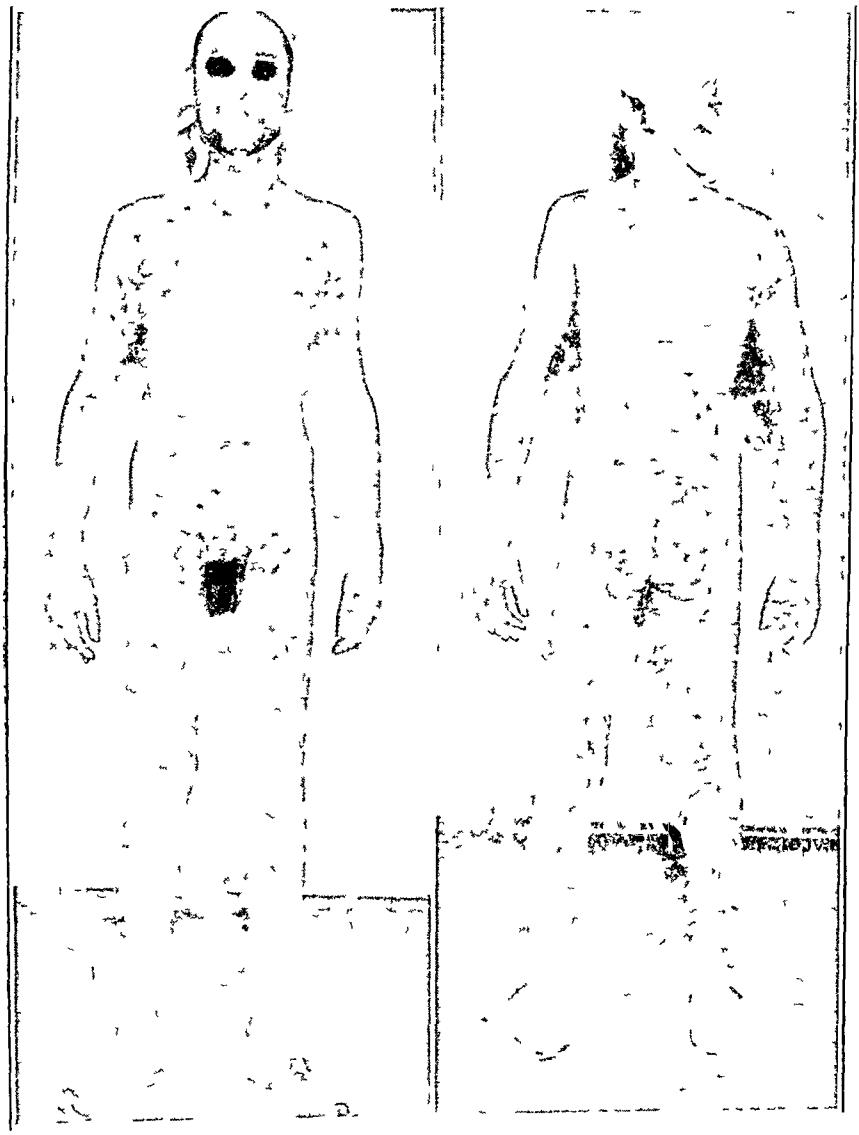


Fig 1 (case 1) —Showing generalized disposition of the granulomatous eruption

sized crusts of the type seen in impetigo contagiosa on all parts of the cutaneous surface Aside from the previously described lesions, many of which could have represented a secondary pyoderma, there were numerous efflorescences of a different type There were pea-sized to large coin-sized, discrete, brown-red plaques elevated to 3/16 inch above the surface of the surrounding skin Some were slightly rounded, while others were flat topped, with precipitous sides

plus five injections of bismuth subsalicylate, in a period of eight days On her first admission she named 2 contacts, both were unavailable to us, but they were reported to the state health department At the beginning of treatment, strongly positive reactions were obtained to the Kolmer complement fixation test and to the Kahn, Kline and Mazzini flocculation tests Titers in the quantitative Kline and Mazzini tests were 16 and 32 dilution units, respectively, in the Kolmer test, 16 dilution units A consistent decline in reagin titer was observed in regular monthly repetitions of these four tests in July, August, September, October, November and December On December 10, the reaction to the Kolmer test was negative and that to the Kahn test was doubtful, the Kline and Mazzini tests indicated 1 unit each On Jan 3, 1946, the results were the same On February 8, the reaction to the Kline test was doubtful, the Mazzini test indicated 1 flocculation unit, and reactions to the Kolmer and Kahn tests were negative Two months later, on April 2, reactions to the Kolmer, Kahn and Mazzini tests were negative and the reaction to the Kline test was doubtful One month later, on May 3, and again on June 3, all four tests gave negative results

On July 15, one month and twelve days later reactions to all four tests were strongly positive (64 Kolmer units, 32 Kline units and 64 Mazzini units, and the titer in the quantitative Kahn test, 256 units) There were dark field-positive condylomas on the vulva A diagnosis of secondary syphilis was made, and the patient was retreated with the schedule of treatment used for the original infection (1,200,000 units of penicillin and five injections of bismuth subsalicylate) Examination of the spinal fluid gave normal results at that time Clinical and serologic response to treatment was normal in every respect, the titer for the quantitative Kahn test having dropped during the following two months from an original level of 256 units to one of 32 units and during the next three months to the point where serodiagnosis was doubtful Reactions to all four tests were negative in the sixth month following the second treatment and have remained so to the time of this report

A history of contacts obtained on July 15 was as follows Three Negro soldiers were named as contacts during the preceding three months, but objective data on these persons were not available In the work at the Dallas Syphilis and Venereal Disease Clinic, an extremely high incidence of the disease has been noted in Negro soldiers

Undeniably promiscuous, the patient could have had a seronegative primary lesion on the cervix as early as June 3, but a dark field examination of the cervix was not made on that date Although, because of a lack of data on contacts and clinical and serologic observations between June 3 and July 15, this patient is classified as having had a relapse, the typical satisfactory response to a second course of treatment should, in our opinion, classify her as having been reinfected

SUMMARY

In this study, 1,105 patients with early syphilis (primary or secondary) were treated with penicillin, five different treatment schedules were used, and the observation periods ranged from nine months to three and a half years

One hundred and thirty-seven of these patients later exhibited evidence of infectious relapse ("infectious failure")

For 80 of the 137 patients the diagnosis of reinfection was made, and 57 were left in the category of infectious relapse

Treatment with mild local antiseptics, such as potassium permanganate, silver nitrate and tyrothricin solutions and ammoniated mercury, was instituted, together with injections of penicillin and supportive measures, as well as potassium arsenite

TABLE 1.—*Examinations of the Blood*

Date	Red Blood Cells	White Blood Cells	Polymorphonuclear Cells	Lymphocytes	Eosinophils
7/ 6/46	4,780,000	22,700	60%	28%	12%
7/ 8/46	5,010,000	37,500	59%	21%	20%
8/ 1/46	4,480,000	19,000	40%	22%	38%
8/ 2/46	4,040,000	15,000	26%	25%	49%
8/ 5/46	4,630,000	39,000	16%	21%	63%
	Cough and increased breath sounds				
8/ 6/46	4,740,000	50,600	20%	12%	66%
8/ 7/46	4,860,000	56,000	20%	33%	47%
8/ 8/46	4,600,000	48,000	14%	28%	56%
8/ 9/46	5,120,000	42,200	35%	17%	48%
8/10/46	4,870,000	35,000	16%	30%	54%
8/13/46	5,000,000	32,400	32%	28%	40%
8/14/46	5,100,000	25,500	34%	24%	42%
8/15/46	4,980,000	22 300	28%	27%	45%
8/17/46	4,430,000	28,300	30%	14%	56%
8/19/46	4,490,000	37,000	12%	24%	64%
8/20/46	5,040,000	39,600	30%	27%	43%
8/21/46	5,090,000	34,400	23%	15%	62%
8/22/46	5,030,000	32,900	23%	19%	58%
	Roentgenogram of the chest clear				
	Roentgen ray treatments started				
10/31/46	5,120,000	22,000	35%	20%	45%
11/ 1/46	5,120,000	22,400	31%	27%	42%
11/ 2/46	4,870,000	13,000	36%	18%	46%
11/ 4/46	5,140,000	12,200	49%	31%	20%
11/ 5/46	5,100,000	19,500	24%	28%	48%
11/ 6/46	5,050,000	12,000	28%	39%	28%
11/ 7/46	5,030,000	10,900	31%	45%	24%
11/ 8/46	4,750,000	8,400	38%	28%	34%
11/ 9/46	5,090,000	7,700	30%	40%	30%
11/11/46	4,740,000	9,700	50%	33%	17%
11/13/46	4,750,000	9,100	56%	26%	18%
11/14/46	4,250,000	6,800	44%	50%	6%
11/15/46	5,000,000	7,400	53%	36%	11%
11/18/46	4,100,000	6,000	36%	36%	28%
12/ 9/46	5,450,000	10,400	49%	21%	27%
12/19/46	5,300,000	7,500	33%	38%	22%
1/ 6/47	5,100,000	7,400	31%	48%	21%
1/ 9/47	5,000,000	6,000	33%	42%	25%
	Last roentgen irradiation given				

solution U S P (Fowler's solution) This therapy produced some amelioration of the manifestly pyogenic component of the cutaneous picture, but little other change Fever continued, with the temperature reaching a peak of 100 to 101 F each day Old lesions of the vesicular type continued to regress and new ones to appear, and the plaques became a little smaller and cleaner but were otherwise unchanged

EOSINOPHILIC GRANULOMAS OF THE SKIN

EDWARD A OLIVER, M D

JAMES R WEBSTER, M D

JULIUS E GINSBERG, M D

AND

H S STEINBERG, M D

CHICAGO

DURING the past few years the attention of American dermatologists has been directed toward a rather wide variety of cutaneous lesions which have been difficult to catalogue in the previously accepted classifications of disorders of the skin but which have in common a granulomatous aspect and structure in which .are found, on histologic examination, a striking number of eosinophils As a purely descriptive convention, it has been convenient to adopt a term which was first used by Nanta and Gadrat,[1] in the European literature, namely, eosinophilic granulomas of the skin

Lewis [2] was the first to present a case under this title in this country, and Weidman [3] and Lewis and Cormia [4] read excellent articles on this unusual condition before this association in 1946

A study of the cases which have been reported with this designation reveals such variations with respect to appearance, course and association with other findings that it is readily apparent that the term cannot be employed to imply a clinical or etiologic entity

The earlier European literature has been thoroughly reviewed by Lewis and Cormia, Lever [5] and Buley [6] It would therefore be

Read at the Sixty-Eighth Annual Meeting of the American Dermatological Association, Inc, San Diego, Calif, April 27, 1948

1 Nanta, A, and Gadrat, J Sur un granulome eosinophilique cutané, Bull Soc franç de dermat et syph (Réunion dermat, Strasbourg) **44**·1470-1479 (July) 1937

2 Lewis, G M A Case for Diagnosis (Erythema Nodosum), Arch Dermat & Syph **48** 436-437 (Oct) 1943, A Case for Diagnosis (Eosinophilic Granuloma?), ibid **49** 375-376 (May) 1944

3 Weidman, F D The "Eosinophilic Granulomas" of the Skin, Arch Dermat & Syph **55** 155-175 (Feb) 1947

4 Lewis, G, and Cormia, F E Eosinophilic Granuloma Theoretic and Practical Considerations Based on the Study of a Case, Arch Dermat & Syph **55** 176-193 (Feb) 1947

5 Lever, W F Eosinophilic Granuloma of the Skin Its Relation to Erythema Diutinum and Eosinophilic Granuloma of the Bone, Report of a Case, Arch Dermat & Syph **55** 194-211 (Feb) 1947

6 Buley, H M Eosinophil Granuloma of Skin, J Invest Dermat **7** 291-300 (Dec) 1946

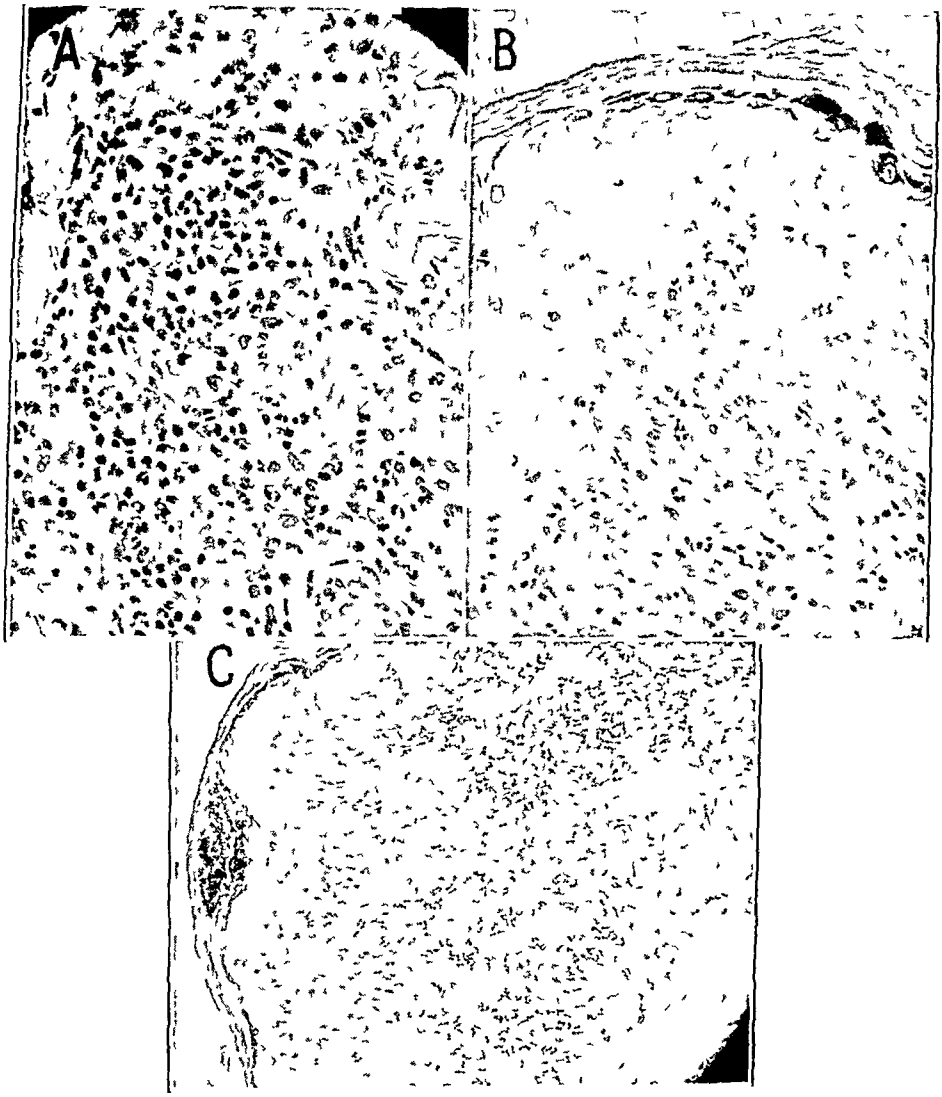


Fig 3 (case 1) —*A*, high power magnification of lower right corner of section 1 Eosinophils were much denser and more prominent in certain other areas *B*, view with high power mganification showing invasion of epidermis by eosinophils and neutrophils *C*, low power view showing nature of infiltrate in dermis, irregular acanthosis, invasion of epidermis by eosinophils and neutrophils and superficial microabscesses

TABLE 2—*Roentgen Therapy* *

	Region Treated	Roentgen Units	Kv	Filter (Mm) Cu	Size of Field (Cm)	Ma	Time (Min)
10/30/46 to 1/9/47	Pelvis, right anterior part	600	140	0 5	15 × 12	20	8 5
	Pelvis, left anterior part	600	140	0 5	15 × 12	20	8 5
	Pelvis, right posterior part	600	140	0 5	15 × 12	20	8 5
	Pelvis, left posterior part	600	140	0 5	15 × 12	20	8 5
11/5/46 to 1/7/47	Upper part of abdomen, right anterior	600	140	0 5	20 × 15	20	8 5
	Upper part of abdomen, left anterior	600	140	0 5	20 × 15	20	8 5
	Upper part of abdomen, right posterior	600	140	0.5	20 × 15	20	8 5
	Upper part of abdomen, left posterior	600	140	0 5	20 × 15	20	8.5

* Each field received only 150 r at each treatment and no area was treated oftener than every ten days

In constrast to the aforementioned numerous and wide discrepancies, there is one rather definite similarity in the different cases reported, namely, that, whenever used, radiotherapy has given excellent results in the generalized cases

The previous observations must inevitably lead to the question Is there at present a still poorly defined entity which might be designated as eosinophilic granuloma of the skin and which might have possible relation to eosinophilic granuloma of bone and other reticuloendothelioses, or does a pronounced eosinophilic response of varied cause not infrequently complicate different disease entities so that their essential nature may become poorly recognizable? It is, of course, conceivable that both of these possibilities may prove to be true

It is felt that the answer or answers to this question can be gained eventually only through the pooling of all information concerning such observations, and toward this end our 2 cases are presented As will be readily apparent, they are quite different from each other, but each is similar to cases which have been reported as cases of eosinophilic granuloma of the skin

REPORT OF CASES

CASE 1—*History*—H B, a 26 year Jew, in December 1945 first noticed pustular lesions of the skin, associated with moderate general weakness Past personal and family medical histories were irrelevant, with the possible exception of the fact that a sister "has hay fever and asthma"

The cutaneous lesions had appeared while the patient was at home in Iowa two months after his discharge from the Army During his period of military service he had been in the Caribbean area for a short time, but otherwise he had never been outside the continental United States The earliest efflorescences had been pin-sized pruritic papules on the chest, shoulders and upper portion of the abdomen, soon followed by similar ones, which became vesicular, in the inguinal and crural areas Treatment with sulfonamide drugs by mouth and with a moderate amount of penicillin by injection failed to affect the process, and new lesions continued to appear In February 1946, the patient entered the Veterans Administration Center at Des Moines, Iowa There he received symptomatic local treatment, together with tonic and supportive measures, including liver, and considerable penicillin and streptomycin by injection, all of which proved ineffective The condition of the skin became worse and the weakness more pronounced, and considerable malaise developed

On June 25, 1946, he was admitted to the Section on Dermatology of the Veterans Administration Hospital at Hines, Ill Examined at that time, approximately six months after the onset of symptoms, he proved to be a somewhat emaciated person, who appeared acutely ill, had a definite tachycardia and a temperature of 100 4 F (fig 1) The chief complaints were weakness and severe itching associated with the cutaneous eruption At no time previous to or during the period of observation were there any symptoms referable to the skeletal system, nor was there any polyuria or polydipsia

Initial Examination—General physical examination revealed essentially normal conditions except for those of the skin Specifically, the liver and spleen did not

a total of 600 r The areas treated were the pelvis, the right and the left side anteriorly and posteriorly, and the hypochondrium, the right and the left side anteriorly and posteriorly The aforementioned areas were treated in rotation until each area had received 600 r Only one area received treatment (150 r) on any day, and no one area received treatment oftener than every ten days The factors used were as follows kilovolts, 140, filter, 0 5 mm of copper, milliamperes, 20, time, 8 5 minutes, and dose per treatment, 150 r

The patient also had a moderate amount of fractional superficial roentgen ray treatment to individual cutaneous areas During this period there was no other treatment used except simple tonic medication and mildly antiseptic local preparations Within two weeks after the beginning of the radiation therapy the cutaneous lesions began to involute, and, as can be seen in table 1, the leukocytosis and eosinophilia showed a distinct downward trend At the time of his discharge from the hospital, on March 1, there were no active cutaneous lesions, although pigmented relics persisted and the patient had experienced several episodes of mild urticaria, which could have been psychogenic The cytologic picture of the blood had been normal for approximately one and a half months Another sternal puncture, on January 9, revealed a preponderance of eosinophils but no abnormal elements The patient had gained appreciably in weight and had completely regained his strength (fig 4)

Since then he has been seen three times, at intervals of several months, as an outpatient and has been presented again before the Chicago Dermatological Society There has been no recurrence of the cutaneous picture described, although in the fall of 1947 the patient had an episode of urticaria, for which he was treated elsewhere He has felt well generally and has had no return of the weakness On each of our observations, the last of which was on Jan 26, 1948, blood counts were within normal limits and roentgenograms of the chest showed no pathologic changes

Case 2.—The patient was a white man aged 42, who first noticed a few dark, cherry red, plaquelike lesions on his face in January 1943 The lesions developed slowly, and the patient was kept under observation in a naval dispensary A biopsy was performed in September 1943, and another in March 1944 On both occasions the pathologic diagnosis was "chronic inflammation, probably mycosis fungoides"

From October to December 1943 the patient received eight roentgen ray treatments of 75 r at weekly intervals After completion of this treatment the lesions flattened and changed color from cherry red to a light brown However, three months after the roentgen ray treatment was completed, the lesions became active again and showed occasional activity from then until the time of writing

At the time of writing there was a rectangular patch on the left cheek, measuring 1¼ inches by ¾ inch, another rectangular patch in front of the right ear, measuring 1½ inches by 1 inch, a quarter-sized patch in the right temporal region, and another patch of the same size on the right cheek These lesions are not elevated, are reddish brown and appear yellowish brown on pressure with a diascope They are not pruritic A general physical examination showed nothing abnormal The roentgenograms of the chest showed no evidence of pathologic changes (fig 5)

The urine was normal The blood showed a hemoglobin content of 87 to 90 per cent The color index was 0 9 There were 4,500,000 red blood cells and 6,000 to 9,600 white blood cells, the differential count was as follows neutrophils,

Their surfaces were rather vegetative in appearance, and many of them were covered with dirty brown crusts, under which the surface was superficially eroded and covered with a foul-smelling mucoid pus Although a few such lesions were widely scattered, the majority were grouped in the axillas, the genitocrural and the gluteal regions and on the face, scalp and proximal portions of the extremities Apparently some lesions of this type had involuted, leaving virtually no atrophy or scarring, but rather patches of either relative depigmentation or light brown hyperpigmentation (fig 2) The lesions on the scalp did not produce notable alopecia, even of temporary nature

Laboratory findings at this time were as follows Urinalysis showed normal values Reactions in the Wassermann and the Kahn tests were negative The red blood cell count was 3,500,000 per cubic millimeter, with hemoglobin, 11 Gm There were 15,800 white blood cells per cubic millimeter, and the differential blood count



Fig 2 (case 1) —Showing distribution and character of lesions on thighs

was as follows polymorphonuclear neutrophils, 64 per cent, lymphocytes, 23 per cent, and polymorphonuclear eosinophils, 13 per cent The sedimentation rate (Cutler) was 15 millimeters per hour There was 30 mg of nonprotein nitrogen, 1 3 mg of creatinin, and 93 mg of sugar per hundred cubic centimeters The total protein was 6 9 mg per hundred cubic centimeters (3 4 mg of albumin and 3 5 mg of globulin) Reactions in agglutination tests for the typhoid-paratyphoid group and Proteus vulgaris (Bacillus proteus) X_{19} were negative

Roentgenologic study of the chest revealed no abnormalities Cultures of the cutaneous lesions produced no fungi, but showed the presence, in all types of active lesions, of hemolytic staphylococci

Subsequent Investigation and Course—At this time suggestions for possible diagnosis included dermatitis herpetiformis, pemphigus vegetans and mycosis (granuloma) fungoides or some other form of lymphoblastoma

infiltrate from the dermis Eosinophils and neutrophils predominated in certain areas of the infiltrate, and the lymphocytic types of cells in others The lymphocytic cells had no mitotic figures (fig 6)

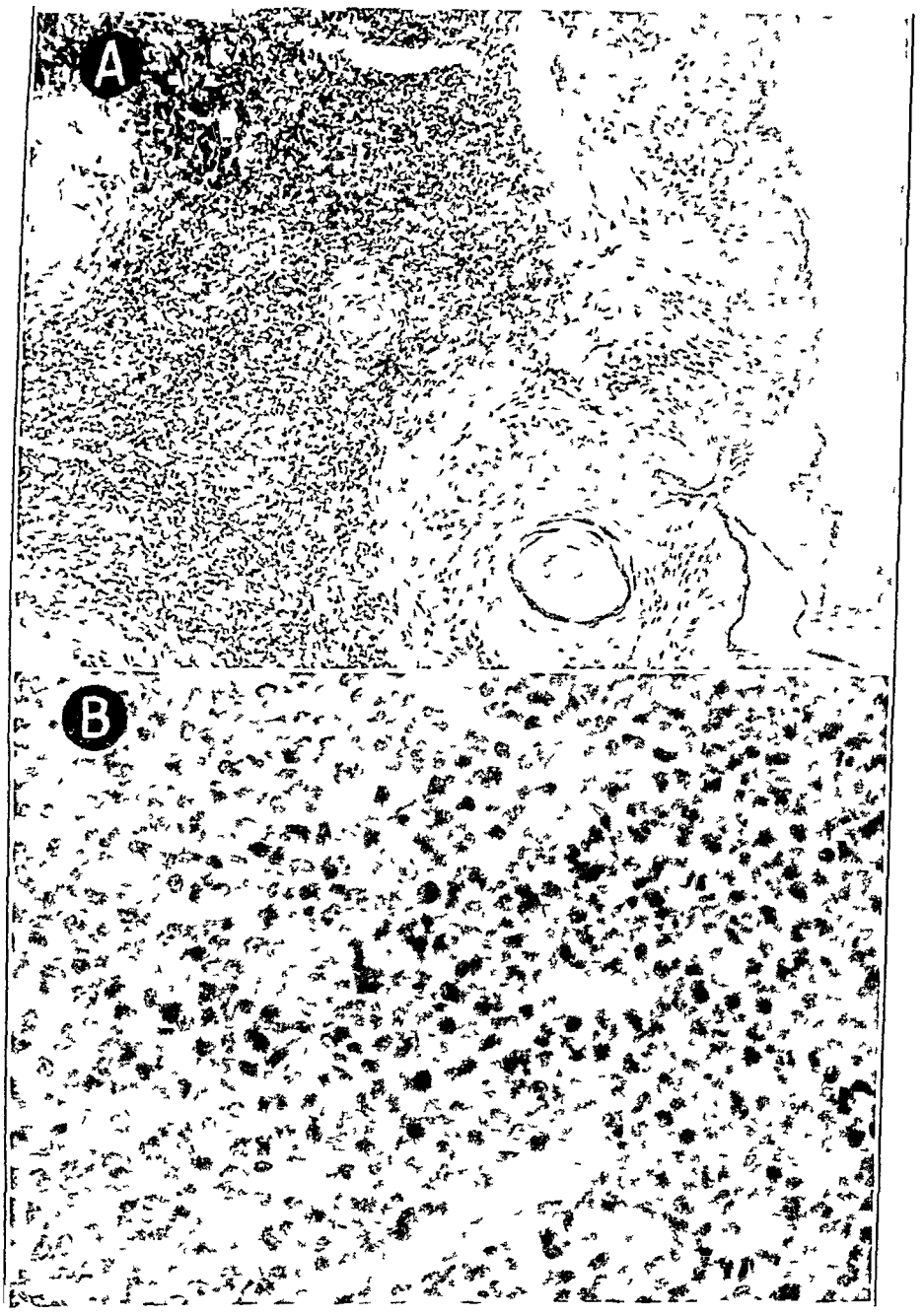


Fig 6 (case 2) —*A*, low power view showing mild irregular acanthosis and tumor-like infiltrate in the dermis *B*, photograph with high power magnification showing polymorphous nature of dermal infiltrate Eosinophils are prominent

SUMMARY

Two cases of eosinophilic granuloma of the skin are reported They are entirely different in their clinical characteristics, and yet histologic

A blood culture was reported as showing the presence of the gram-negative Aerobacter aerogenes and a gram-positive nonhemolytic staphylococcus These findings could not be confirmed and were interpreted as being the result of contamination Nevertheless, the patient received streptomycin, 2 Gm daily for seven days,' which also failed to produce any significant change

Starting about July 6, two weeks after admission, the patient exhibited a gradually increasing eosinophilia of the blood with an accompanying leukocytosis (table 1)

Examinations of the stools at this time, and repeatedly thereafter, did not reveal blood and intestinal parasites, and cultures showed no unusual bacteria Early in August the patient exhibited a slight cough, and was still having a daily rise in temperature to slightly above 100 F Pulmonary findings were negative except for slightly exaggerated breath sounds, but examinations of sputum and roentgenograms of the chest were made The sputum contained a moderate number of eosinophils, but no fungi or tubercle bacilli were found on repeated examinations The roentgenogram of the chest taken on August 9 revealed "soft shadows of increased density in both lung fields" which to the roentgenologist at first suggested fungous infection but was later interpreted as being compatible with the appearance in Loffler's syndrome Another film made on August 22 showed virtually complete return to normal, and repeated reexaminations since that time have shown no abnormalities There was subsequent slight decrease in the leukocytosis and eosinophilia after this date, but the figures still remained far above normal

After repeatedly refusing, the patient finally consented to sternal puncture and biopsy of the skin The former, done on August 16, revealed a hyperplastic bone marrow containing all elements normally present but showing no evidence of leukemia

Histopathologic Changes—A biopsy specimen of a representative elevated, partially crusted granulomatous lesion on the flexor surface of the forearm was taken on August 16 Sections of the specimen stained with hematoxylin and eosin showed an irregular acanthosis and edema of the epidermis The epidermis was invaded and partially replaced at certain points by cells of the infiltrate from the dermis There were superficial epidermal microabscesses containing polymorphonuclear eosinophils and neutrophils Most of the upper portion of the dermis was filled with cellular aggregates consisting of polymorphonuclear eosinophils, neutrophils, fibroblasts, histiocytes and undifferentiated connective tissue cells In the cellular aggregates there were many small, newly formed blood vessels The cells of the infiltrate, both in the epidermis and the dermis, were predominantly polymorphonuclear eosinophils and neutrophils, the proportion of eosinophils at some points being over half of the total number of cells in the infiltrate The small, newly formed blood vessels also showed a prominent content of eosinophils The Van Gieson-Weigert stain showed a loss of elastic tissue only in the densely infiltrated areas Silver stains showed no increase in reticulum fibers (fig 3)

During the next two months, with the patient on a schedule of rest and supportive treatment, along with acetarsone N F (stovarsol®) by mouth according to the schedule proposed by Oppenheim,[9] the edema of the extremities subsided and the vesicular component of the skin eruption disappeared, although the plaques remained unchanged The patient felt better and stronger, although he continued to exhibit a mild daily elevation in temperature and there was no significant change in the blood picture

9 Oppenheim, M, and Cohen, I Acetarsone in the Treatment of Pemphigus, Arch Dermat & Syph **47**.40 (Jan) 1943

There is one more phase that I should like to discuss, namely the status of the reticuloendothelial reaction in the idiopathic cases, about which I am not satisfied In some cases it is inflammatory in nature and in others leukotic I cite particularly the question of the presence or absence of monocyte activity Monocytes are extremely difficult to identify in paraffin-embedded sections, even when they are stained by the Giemsa technic Even with the best stain, time and time again the matter cannot be decided I think that all present recall Dr Winer's communication in respect to the usefulness of impression preparations in Hodgkin's disease for studying details of leukotic cells

DR C F LEHMANN, San Antonio, Texas The subject of eosinophilic diseases takes one into a good many wide theoretic ramifications I wish to report an experience I had which I believe might be of some help to anyone who encounters such a case That is a case of a 65 year old man who came in with a most pronounced erythema multiforme (*South M J* **41** 37-44 [Jan] 1948) He had a high temperature, and an eosinophil count reaching 79 per cent during the very short course of the illness (fourteen days), a hacking cough developed, and there was swelling of the arms and legs for six weeks Because the cutaneous manifestations predominated, I did not consider eosinophilic disease I tried to call the condition eosinophilic leukemia, and the internist did not agree The disease had a fairly progressive course, and the patient was extremely sick We followed up the case, and three months later the blood count was normal, one year later he had an illness, but by the time I saw him the urticaria had been relieved and his blood count was normal The consideration of the diagnosis led us to include Loffler's syndrome or tropical eosinophilia with cutaneous manifestations In Palestine there have been reports of an eosinophilic disease with cutaneous manifestations In these cases, bone marrow studies showed increased eosinophils The cutaneous eruption varied from erythema multiforme to nodular eruptions, and swelling of the extremities was noted The patient in my case did not have much of a cough The pulmonary infiltration as seen with roentgen rays was very slight These findings plus the fact that Loffler's syndrome does not usually include very high fever was not strongly corroborative of a diagnosis of Loffler's syndrome On the other hand, the course of the disease did not fit in with the characteristics of tropical eosinophilia Wilson and his British colleagues, writing on tropical eosinophilia, found the copra mite in the sputum in a small percentage of cases

This case aroused my interest in eosinophilic dyscrasia and showed me the numerous ramifications of this abnormality It is my opinion that eosinophilic disease must be an allergic manifestation

DR. N P ANDERSON, Los Angeles Referring to this particular pathologic entity of eosinophilic granuloma, I should like to call attention to a recent communication by Dr Allen (*Am J Path* **24** 367-388 [March] 1948) Dr Allen reported 20 cases of persistent insect bites with some lesions lasting for as long as two years These followed the bites of ticks, chiggers and mosquitoes Attention was called to two or three facts which we might mention First, many insect bites ulcerated, healed and then broke down again, and as a result one found pseudo epitheliomatous hyperplasia There also occurred pronounced cellular infiltration in the cutis This infiltrate was very dense and extensive There were present many mature eosinophils and a large number of plasma cells, some of which were multinucleated and simulated the multinucleated cells seen in mycosis fungoides Many histiocytes were found Occasionally there were such

The patient was presented at the October 1946 meeting of the Chicago Dermatological Society as having "possible eosinophilic granuloma of the skin with Loffler's syndrome" There was more or less general agreement with this diagnosis, and, after the discussion, at the suggestion of Dr Paul O'Leary, it

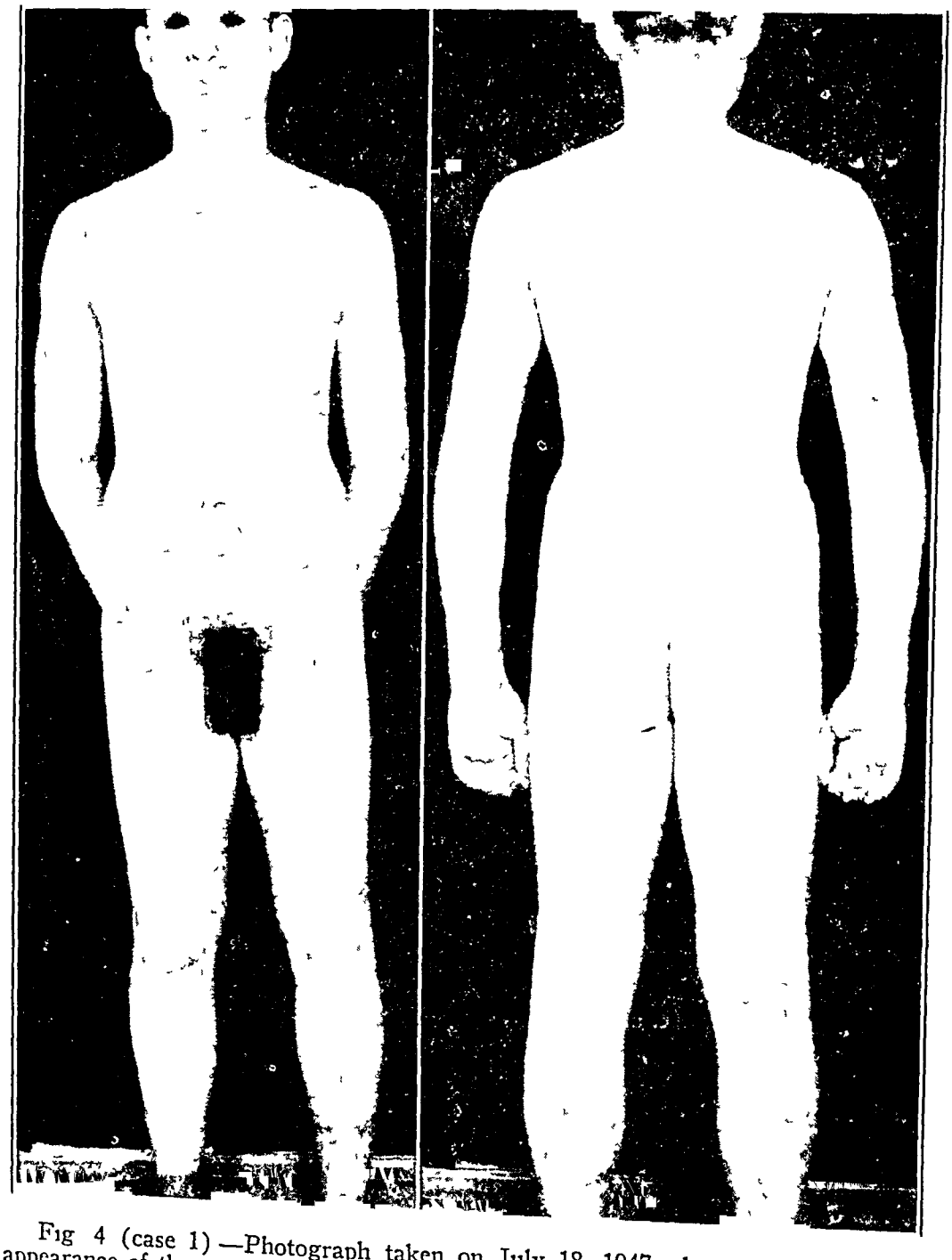


Fig 4 (case 1) —Photograph taken on July 18, 1947, showing complete disappearance of the eruption, improvement in general condition and residual pigmentation of legs

was decided to use roentgen therapy directed toward the main concentrations of the reticuloendothelial system

Accordingly, on October 30, treatment was begun as shown in table 2 This treatment was continued through Jan 9, 1947, until each of the areas had received

received eight roentgen ray treatments of 75 r When we first saw him, we made a diagnosis of possible sarcoid, but histologic examination proved the condition to be eosinophilic granuloma Occasionally, the lesions show a little activity, but there are no subjective symptoms The patient is bothered only by their appearance

Concerning case 1, Dr Weidman asked whether the patient had a cough He had no cough until about the first part of August There was some history of hay fever in the family, and there were eosinophils in the sputum

I read Dr Fred Lehman's paper with interest His case was one of erythema multiforme with Loffler's syndrome

Dr Lewis mentioned the fact that there may be some connection between eosinophilic granuloma and the Hand-Schuller-Christian disease We believe that there may be Our purpose in presenting this paper was to report 2 more interesting cases of this unique disease in the hope that as more and more cases are reported, we shall obtain more information about the condition

48 to 56 per cent, lymphocytes, from 38 to 46 per cent, and eosinophils, 6 per cent. The sedimentation rate was from 2 to 4 mm per hour. The total protein was 6 9 Gm per hundred cubic centimeters of blood, with an albumin-globulin ratio of 1 7 to 1.

A biopsy specimen of one of the superficially elevated granulomatous plaques on the right cheek was removed. Sections of the specimen stained with hematoxylin

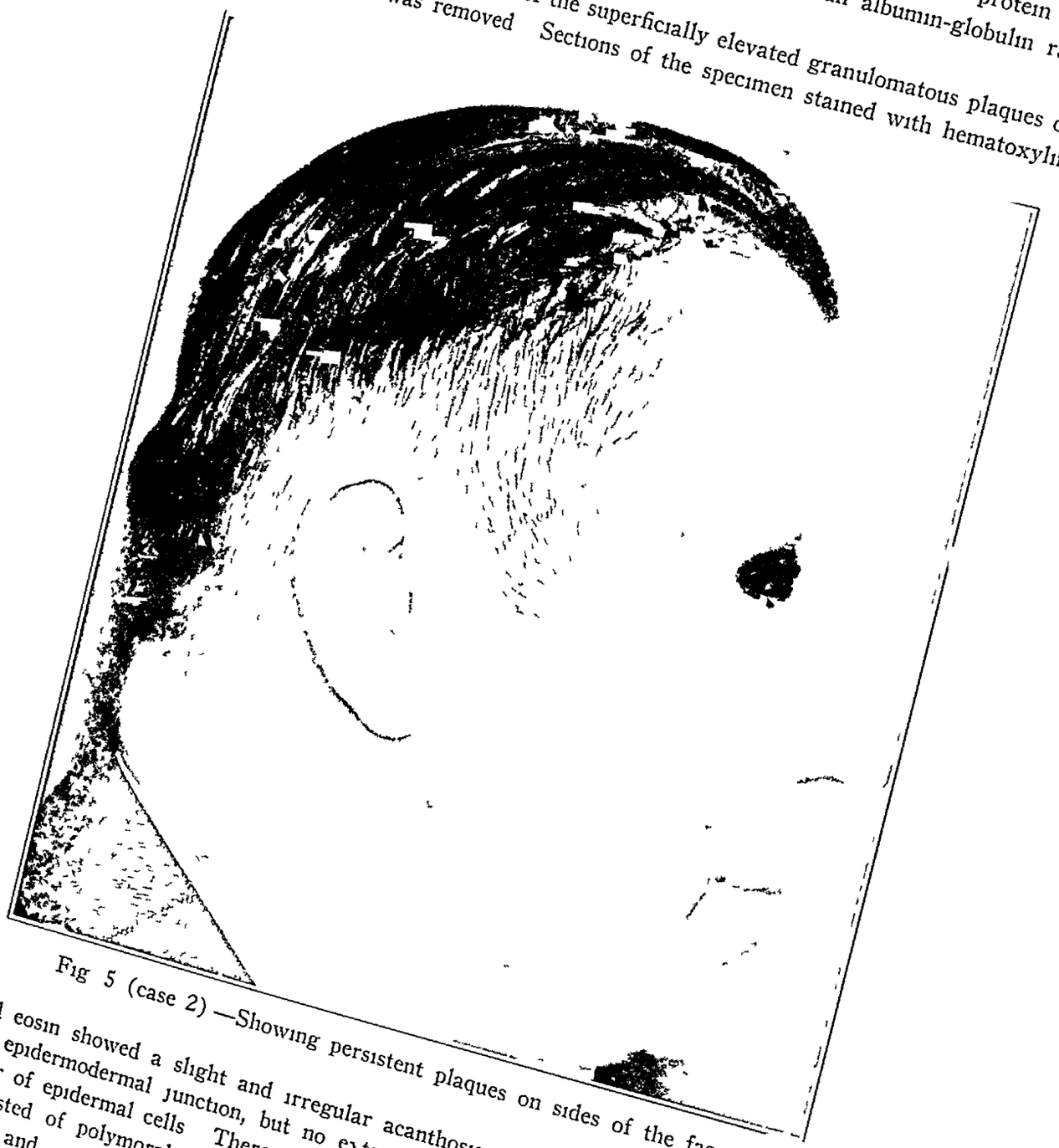


Fig. 5 (case 2).—Showing persistent plaques on sides of the face.

and eosin showed a slight and irregular acanthosis. There was some edema at the epidermodermal junction, but no extensive liquefactive necrosis of the basal layer of epidermal cells. There was a dense tumor-like infiltrate of cells, which consisted of polymorphonuclear eosinophils and neutrophils, lymphocytes, monocytes and connective tissue cells, in the dermis. There was some pyknosis, karyorrhexis and clumping of nuclei. There was no tendency toward abundant formation of new blood vessels or toward an increase in reticulum. A narrow band of dermis equal in thickness to the epidermis separated the tumor-like

the use of radiations for nonmalignant tumors in general Some statements, such as "anyone who has ever had even a single dose of low voltage X-ray applied to the skin is a possible candidate for subsequent skin cancer,"[4] appear fantastic Recently a distressing illustration of an atrophic breast following the use of radium for hemangioma appeared in this journal[5] On the other hand, to quote only two recent papers, Porta[6] studied 245 cases of cavernous hemangioma treated with radiations and found 1 case with atrophy of the jaw, and Pendergrass and associates[7] stated that they had observed their results over a period of twenty years and in no instance had obtained unsatisfactory results attributable to radiation

There is no doubt that at times radium has been used improperly and unnecessarily For instance, in the case of the radioresistant nevus flammeus, and particularly when radium has been used in plaque form, the resultant white, square, scarred areas are much worse looking and more difficult to hide than was the original hemangioma Radium in plaque form has even been used in an attempt to remove common moles, and this treatment has been followed by a white, depressed, square area with the unaffected mole still present in the center[8]

The purpose of this paper is to point out the fact that although cases of unpleasant sequelae from the use of radiations for hemangioma are encountered, there have been any number of similar cases in which there has been successful treatment with radiations without any demonstrable trace of damage to the skin or underlying structures This observation indicates that the fault does not lie entirely with the radiations Mistakes will always be made, and they are likely to be noticed and emphasized when the unpleasant sequelae are located on visible structures Condemnation of a therapeutic method because of some mistakes in its use is unjustified

4 Adair, cited by Sulzberger, M B, and Baer, R L The 1947 Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc, 1948, p 151

5 Underwood, G B, and Gaul, L E Disfiguring Sequelae from Radium Therapy Result of Treatment of a Birthmark Adjacent to the Breast in a Female Infant, Arch Dermat & Syph **57** 918 (May) 1948

6 Porta, C Esiti a distanza della radioterapia degli angiomi (250 casi), Radioterap, radiobiol e fis med **1** 160, 1946

7 Pendergrass, E P, Katterjohn, J C, and Butchart, J B Some Considerations in the Treatment of Hemangioma in Infants and Young Children, Am J Roentgenol **60** 182, 1948

8 Ronchese, F Occupational Marks and Other Physical Signs A Guide to Personal Identification, New York, Grune & Stratton, Inc, 1948, p 142

examination of biopsy specimens taken in each case show polymorphonuclear eosinophilic infiltrates and granulomatous tissue changes which we believe are compatible with those seen in eosinophilic granulomas of the skin

The patient in case 1 exhibited a generalized eruption, and during the course of his illness the signs of Loffler's syndrome developed He continually showed a decided leukocytosis, with an eosinophil count as high as 66 per cent

Under treatment with roentgen radiation directed toward the main concentrations of the reticuloendothelial system he began to show improvement, and after he had finished his course of treatment all his cutaneous lesions disappeared and in a short time his blood counts returned to normal When he was last seen by us, on Jan 6, 1948, almost a year after his discharge from the hospital, his skin was clear, blood counts were within normal limits and roentgenograms of the chest showed no pathologic changes

The patient in case 2 displayed lesions on the face much like those in the cases described by Buley in 1945 and in that reported by Lever in 1947 While in the Navy he received radiotherapy His condition has remained unchanged

55 East Washington Street

122 South Michigan Avenue

826 East Sixty-First Street

366 West Adams Street

ABSTRACT OF DISCUSSION

DR. FRED D WEIDMAN, Philadelphia Two years ago I submitted a catalogue and classification of the 20 cases that I could collect in the hope of stimulating interest in the subject It was not a new one, but the American literature did not contain adequate information about it Since then, a number of sections have been sent to me which I judged to be of eosinophilic granuloma of the skin, now Dr Oliver reports 2 cases, and Dr Curtis recently reported a case which included bone involvement In short, the subject is being actively pursued

Today I wish to discuss the position which Dr Oliver's 2 cases might occupy in the classification which I submitted at that time I hope that I made it clear in my paper that it is only a temporary classification It will probably be radically modified and some of the cases thrown out As I see it, Dr Oliver's 2 cases would qualify for temporary addition to the list of 20 With respect to case 1, I should like to ask Dr Oliver whether there were any eosinophils in the sputum The patient had bronchial asthma, and cough is usually regarded as a symptom I expected to see a rather larger shadow, a more definite tumor Did the roentgenologists feel that the area was in fact a tumor? As regards case 2, I think that the lesions seen in it are the type that give the most promise of emerging as clinically recognizable eosinophilic granuloma of the skin Dr Nelson Paul Anderson will have something to say, too, about his case, which falls into this same category His case raises the count to 4 of which I know, which is a good showing

to four hours, at intervals of six to eight weeks, from one to ten times, the hemangioma being surrounded by 1 mm of lead foil

Among the patients who had received radium treatment for cavernous hemangiomas in various body areas from ten to fifteen years previous to this study, 28 were reexamined for external appearance, scars, deformities and skeletal damage by comparison of the treated area with the untreated one on the opposite side This was done with the cooperation of Dr Lawrence A Martineau, Director of the Department of Roentgenology of the Rhode Island Hospital

REPORT OF CASES

CASE 1.—A baby girl, aged 6 months, with a cavernous hemangioma on the right breast, on Aug 7, 1937 received one treatment of 75 milligram hours (three 25 mg radium tubes, for three hours, at 1 cm from the skin) The patient was seen again on Nov 29, 1948 Remnants of the hemangioma were represented by

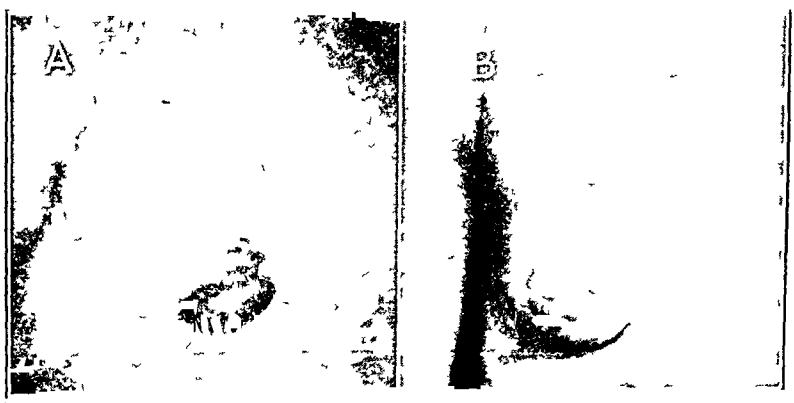


FIG 2.—Cavernous hemangioma of the right breast, when the patient was at the age of 6 months (*A*) and at the age of 12 years (*B*) On Aug 7, 1937, treatment with radium, 75 milligram hours, was given Only a wrinkly, slightly boggy, soft scar is present No apparent damage is detectable in the breast or the underlying structures

an area of soft scar, and the treated breast was slightly larger than the other (fig 2) No skeletal abnormalities were detectable This case is particularly suited to comparison with the one reported by Underwood and Gaul [5] Today, if I had a similar case, I should consider expectant therapy first and sclerosing injections second I should consider radiations unnecessary, and hence contraindicated. However, this case shows that radiations can be used without demonstrable harm

CASE 2.—A baby boy was treated at the age of 6 months with 1,500 milligram hours (one 50 mg radium tube, at 1 cm distance, for three hours, ten times, at two month intervals) At the time of writing the patient is 12 years old, the lip appears normal (fig 3), except for the indentation left by the original lesion There is no evidence of bony or dental pathologic changes in either jaw

Other patients with infantile cavernous hemangiomas of the left arm, of the right forearm, of the proximal phalanx of the right index

observations as epidermal cysts, and in 1 case a portion of the tic was found in the center of such a cyst This production of eosinophilic granuloma by insect bites seems worthy of comment

DR FRANCIS A ELLIS, Baltimore One of Dr H M Robinson Sr's cases, which was reported by Dr Weidman in 1946 as an example of eosinophilic granuloma, has now been followed up for three years The lesion appeared first on the corona and later extended up the urethra and to the perineal region An enlarged inguinal lymph node, which was later removed, developed The white cell count averaged about 15,000, with 60 per cent eosinophils The cutaneous lesions, lymph nodes and bone marrow obtained by puncture all showed a similar percentage of eosinophils The pathologists were unwilling to accept the condition as eosinophilic granuloma but considered the cutaneous lesions to be angioma, apparently an unusual form of Kaposi's disease (xeroderma pigmentosums), in which there was endothelial proliferation, with large numbers of eosinophils

DR HAMILTON MONTGOMERY, Rochester, Minn I have had the opportunity of studying the microscopic sections of the cases presented by Dr Oliver and his associates In 1 of his cases in which eosinophilia was present there was no histologic evidence of mycosis fungoides About 40 per cent of the cases of mycosis fungoides as reported in the literature, however, include eosinophilia The characteristics seen in the sections in case 1 closely simulate the changes seen in pemphigus vegetans, including pseudoepitheliomatous hyperplasia and microabscess formation with a dense infiltrate of eosinophils This picture is almost diagnostic for pemphigus vegetans Eosinophilia, of course, is seen in various types of allergic dermatitis, in dermatitis herpetiformis and in association with cutaneous manifestations due to animal parasites Therefore, a diagnosis of eosinophilia of the skin must be qualified, the decision dependent on other associated symptoms and findings I believe that eosinophilic granuloma of the bone and skin should be separated for the time being from eosinophilic granuloma of the skin alone In the latter group, there are, at one extreme, those cases associated with allergic phenomena, including those simulating periarteritis nodosa, such as Lewis's case, and, at the other, those related to lymphoblastoma, especially Hodgkin's disease, as were some of Weidman's cases

DR GEORGE LEWIS, New York Just a word about a patient with eosinophilic granuloma presented before this association[4] The patient, as those present may recall, had a chronic dermatophytosis due to Trichophyton purpureum This patient's lesions were resistant to roentgen irradiation He was given large doses of potassium iodide by mouth for many months Eventually he went on to an apparent cure, as he has not had lesions during the past year Mallory stated the belief that eosinophilic granuloma is nothing more than a benign form of the Hand-Schuller-Christian disease It would seem that the Letterer-Siwe syndrome is a severe manifestation of the same group of diseases During the past year we studied another patient with eosinophilic granuloma The lesions were present in the groins and the axillas and were moist and granulomatous, resembling those in dermatitis vegetans Many histologic sections were studied The changes were consistent with those seen in eosinophilic granuloma This patient had been under observation for fifteen years for diabetes insipidus There also was other evidence of pituitary dysfunction Because of the associated disturbances, it has been difficult to classify the cutaneous disorder

DR. EDWARD A OLIVER, Chicago Case 2 was diagnosed in the Navy as mycosis fungoides, and the patient was treated with roentgen radiation He

EARLY REACTIONS FOLLOWING ROENTGEN RAY EPILATIONS

I ZUGERMAN, M D
PHILADELPHIA

SUBSEQUENT to roentgen epilations, in the treatment of ringworm of the scalp (tinea capitis), early reactions sometimes develop in children [1]

These reactions are as follows

(*a*) Restlessness

(*b*) Nausea and vomiting

(*c*) Headache

(*d*) Loss of appetite

(*e*) Elevation of temperature

These signs and symptoms have been attributed to

(*a*) Nervous strain and restlessness before and during treatment

(*b*) Excessive quantity of food allowed before or after treatment

(*c*) Excessive filtration of the roentgen rays

(*d*) Relatively high voltage

(*e*) A mild variety of radiation sickness

In the study reported here it was noted that although the reactions were temporary, their importance lay in the fact that they tended to discourage one from using this valuable method of treatment with other children

This study covered a period from January 1946 to January 1949 The patients were divided into seven groups The following factors were standard to all groups

(*a*) The technic described by MacKee and Cipollaro [1] for the treatment of ringworm of the scalp was used

(*b*) The dosage was 300 roentgen units (r) measured by a Victoreen r meter

(*c*) The age of the children treated ranged from 6 to 10 years inclusive

(*d*) The treatment was administered at 9 a m The patients were allowed a light breakfast consisting of warm tea or milk and toast No food was allowed for at least two hours following treatment

(*e*) Nervousness and restlessness were carefully noted during each treatment Most children came to the office with the nervousness that continued throughout the treatment

1 MacKee G M, and Cipollaro, A C X-Rays and Radium in the Treatment of Diseases of the Skin, ed 4, Philadelphia, Lea & Febiger, 1946, pp 347-378

RADIUM IN TREATMENT OF HEMANGIOMA

F. RONCHESE, M D
PROVIDENCE, R I

ACCEPTED methods of handling infantile hemangioma are with radium, roentgen rays, injections of a sclerosing fluid, solid carbon dioxide, high frequency coagulation and surgical intervention, and with no treatment when a spontaneous involution is expected

In the last twenty years practically all my hospital and private patients have been treated either with radium, if the lesions were large and cavernous, or with solid carbon dioxide, if the hemangioma was of the small, superficial, strawberry type Results for the few patients I treated with injections of a sclerosing fluid were not satisfactory, because some severe local reactions occurred and because there was lengthy local discomfort, with consequent family upset I never attempted to keep an infant under an x-ray machine for the required length of time

A recent investigation on their spontaneous involution [1] convinced me that the majority of hemangiomas do disappear spontaneously within four or five years, and that, if size, location, sex and parents' cooperation justify expectant therapy, this should be the line of choice to follow If the hemangioma is large and cavernous or small and easily removable, or if it is located on an exposed part and the parents are unwilling to wait four or five years for a spontaneous involution, the form of active treatment considered the best should be administered

The present trend of opinion seems to be toward discouraging the use of radiations in treatment of hemangioma because of the many reports of late sequelae on the skin and the underlying structures Papers have illustrated atrophy of bones following roentgen or radium therapy [2] Sarcoma arising in irradiated bone was reported by Cahan and associates,[3] of the Memorial Hospital, New York. This important study was immediately distorted by the lay press as a warning against

1 Ronchese, F Hemangiomas Should Treatment Be Expectant or Active? Rhode Island M J **29** 658, 1946, Treatment of Facial Angiomas, Queries and Minor Notes, J A M A **133** 578 (Feb 22) 1947

2 Newcomet, W S Developmental Changes Following Irradiation, Am J Roentgenol **36** 338, 1936 Rushton, M A Effects of Radium on the Dentition, Am J Orthodontics **33** 828, 1947

3 Cahan, W G , Woodard, H Q , Higginbothom, N L , and Coley, B L Sarcoma Arising in Irradiated Bone, Cancer **1** 3, 1948

GROUP 6 This group consisted of 9 patients treated by means of the SP 140 tube, 100 kilovolts being used, with no added filtration

All 9 patients had reactions, which were all severe The percentage of reaction was 100

GROUP 7—This group consisted of 18 patients treated by means of the SP 140 tube, 60 kilovolts being used with no added filtration

Fifteen patients of this group had reactions which were mild to moderately severe The percentage of reactions of this group was 83 3

Percentages of Reactions in Groups Treated with Roentgen Rays of Various Qualities

Group	Quality of Roentgen Rays	Number Treated	Number of Reactions	Percentage of Reactions
	Non Nervous Children			
1	80 kv H V L 0 5 mm Al	55	5	9 1
2	100 kv H V L 1 4 mm Al	124	96	77 1
3	80 kv H V L 1 1 mm Al	42	12	28 5
4	60 kv H V L 1 0 mm Al	36	5	13 9
	Nervous Children			
5	80 kv H V L 0 5 mm Al	28	18	64 3
6	100 kv H V L 1 4 mm Al	9	9	100 0
7	60 kv H V L 1 0 mm Al	18	15	83.3

SUMMARY

Reactions have followed roentgen ray epilations of patients suffering from ringworm of the scalp (tinea capitis) with an uncomfortable regularity [1] A study was therefore made of 312 patients that required this method of treatment for cure

The total group was divided into quiet, cooperative children and nervous, restless ones in order to determine whether nervousness is a factor in these reactions The patients were further divided into seven groups, which were treated with different qualities of roentgen rays, depending on the voltage and inherent filtrations of the tubes used

The study has definitely shown that in nervous, uncooperative children there is a substantial increase of the percentage of reactions and a tendency to more severe reactions

I am in favor of using radium (surface, implants, needles) in selected cases, viz, of large cavernous hemangioma in which the other methods of therapy are contraindicated When other methods, believed just as effective, can be used they should be employed in preference to irradiation

Figure 1 shows an ulcerated cavernous hemangioma of the right labium majus in a 5 month old girl The location was an indication for expectant therapy, even after spontaneous rupture of the hemangioma, a natural process leading to speedier involution However, in this case the ulcerated area was constantly bathed in the baby's urine and screams were provoked at every micturition A couple of months of applications of boric acid ointment failed to change the situation I do not believe surgical intervention should be chosen in such a case Injections of a sclerosing fluid and use of solid carbon dioxide in treat-

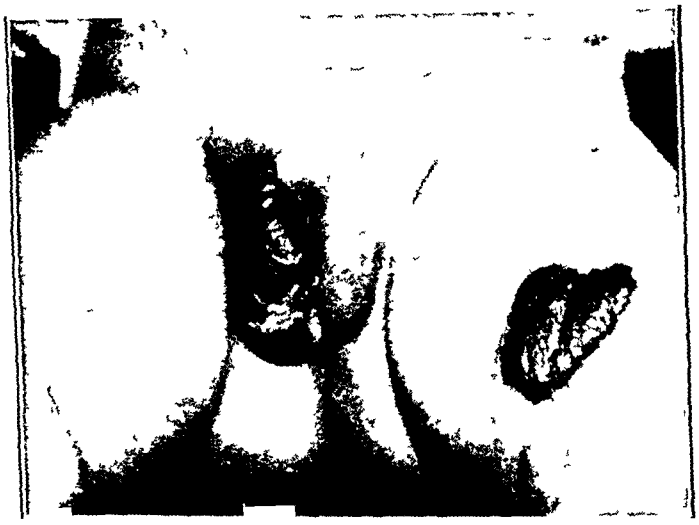


Fig 1—Cavernous hemangioma of the vulva in a 5 month old girl, spontaneously ulcerated and secondarily infected, provoking severe pain at every evacuation of the bladder and not showing signs of involution in spite of the rupture Once the decision has been made in favor of active treatment, I do not believe there is any choice outside of the use of radium The hemangioma on the thigh will not be treated If it has not disappeared spontaneously it can be easily removed surgically after the patient has reached the age of 5 or 6

ment of a ruptured and secondarily infected hemangioma are certainly contraindicated

If expectant therapy is to be abandoned, this case offers an example of a situation in which surface radium therapy or roentgen therapy is the only possible method left to be used

Among 347 miscellaneous hemangiomas seen in the last fifteen years, 89 were treated with surface radium and 5, with radon implants

The surface radium was used in the form of the usual tubes of 25 or 50 mg each, the container representing a filtration of 0 5 mm of silver and 1 mm of brass, held at 1 cm distance from the skin for three

EXPERIMENTAL STUDIES ON TREATMENT OF HUMAN TORULOSIS

ALBERT M KLIGMAN, Ph D, M D
AND
FRED D WEIDMAN, M D
PHILADELPHIA

TORULOSIS is a fatal disease caused by the yeastlike fungus, Cryptococcus neoformans (Torulopsis histolytica, Lodder) The number of reported cases is increasing, and it has become evident that the disease is not as rare as was once thought More than 120 cases are on record,[1] and the 3 unreported cases that are known to us indicate that there are many more

The clinical and pathologic features are primarily those of meningoencephalitis [2] The disease may simulate other disorders of the central nervous system, particularly tuberculous meningitis and tumor of the brain

The disease is worldwide The factors predisposing to infection and the portal of entry are unknown The histopathology has been excellently described [2b]

Treatment has been eminently unsuccessful, the patients usually dying within four to six months after the appearance of symptoms The spontaneous remissions which may occur are usually brief This fact obviously complicates the evaluation of the therapeutic measures in use at the time of the remissions Nevertheless, "cures" have been reported [3] Sometimes patients survive for rather long periods, the

From the Department of Dermatology and Syphilology, University of Pennsylvania School of Medicine, Dr D M Pillsbury, Director

This study was assisted by a grant from the Committee on Therapeutic Research of the Council on Pharmacy and Chemistry of the American Medical Association

1 (*a*) Voyles, G Q, and Beck, E M Systemic Infection Due to Torula Histolytica (Cryptococcus Hominis) Report of Four Cases and Review of Literature, Arch Int Med **77** 504-515 (May) 1946 (*b*) Cox, L B, and Tolhurst, J C Human Torulosis A Clinical, Pathological and Microbiological Study with a Report of Thirteen Cases, Melbourne, Australia, Melbourne University Press, 1946

2 (*a*) Cox and Tolhurst [1b] (*b*) Freeman, W Torula Infection of the Central Nervous System, J f Psychol u Neurol **43** 236-345, 1931

3 (*a*) Marshall, M, and Teed, R W Torula Histolytica Meningoencephalitis Recovery Following Bilateral Mastoidectomy and Sulfonamide Therapy, Preliminary Report, J A M A **120** 527-529 (Oct 17) 1942 (*b*) Toone, E C Torula Histolytica Meningitis Report of a Case with Recovery, Virginia M Monthly **68** 405-407, 1942

finger, of the left shoulder above the scapulohumeral joint, of the left orbital region extending to the left parietal region, of the left wrist, of the left upper portion of the chest, of the outer corner of the left orbital region, of the left upper portion of the chest, of the left side of the neck, of the area above the left breast, of the left shoulder and of the left side of the neck, respectively, when seen from ten to fifteen years after treatment with radium showed no variations of the bony and soft tissues structures on either side

In 16 cases of hemangioma of the scalp in which the patient was reexamined from ten to twelve years after surface radium treatment there was no scar, no loss of hair and no apparent bony pathologic changes



Fig 3—Cavernous hemangioma, with the patient at 6 weeks of age (*A*) and at 12 years (*B*) The tumor received surface treatment with radium (one 50 mg tube, 1 cm from the skin, for three hours, with ten exposures at eight week intervals) The lip appears normal, except for the dent left by the original lesion There is no evidence of bony or dental pathologic changes in either jaw

SUMMARY

In 28 cases of infantile cavernous hemangioma in which there had been treatment with radiations from ten to fifteen years previously the patients failed to show any cutaneous, bony or articular sequelae

These cases are reported to demonstrate that radiation still has its place in the treatment of selected cases of infantile cavernous hemangioma

Between an "all for" radium attitude of some years ago and the present trend of condemnation a happy medium should be arrived at and suitable therapy, including use of radium, selected for each case

170 Waterman Street (6)

invaded than was the brain, however, animals that survived for the longest period almost always showed involvement of the central nervous system, whereas those which died early did not With intravenous injections, with which the survival time was considerably shorter than with intraperitoneal inoculation, the majority of animals apparently did not have involvement of the central nervous system Death is thus not due simply to invasion of the central nervous system In mice, the lung appears to be particularly susceptible In the majority of human patients, also, pulmonary invasion is observed when a careful search is made Occasionally pulmonary tuberculosis is simulated, and diagnosis of this disease has been falsely made more than once [1b]

The frequency with which the organism can be isolated from the blood of infected mice indicates that the blood stream is the vehicle by means of which the disease is disseminated We have also obtained positive blood cultures from infected rats Positive blood cultures have

TABLE 1.—*Distribution of Lesions in Infected Mice Receiving Injections of 8,000,000 Organisms*

Route of Infection	No of Mice	Average Period of Survival, Days *	Percentages of Positive Heart Blood Cultures on Day of Death	Distribution of Histologic Lesions (Percentage of Mice)				
				Brain	Lung	Kidney	Liver	Spleen
Intraperitoneal	12	18 4	83	58	100	70	17	33
Intravenous	12	11 3	66	33	92	66	8	33

* Three mice in the group inoculated intraperitoneally failed to die within the experimental period All the mice inoculated intravenously died

been reported in some cases of human torulosis,[8] and it would seem worth while to add culture of the blood to the routine clinical studies

One further incidental observation may be made When rats were inoculated intraperitoneally, a significant number of animals survived the period of study and were killed after three months Curiously enough, in several of the surviving animals, large, tumor-like masses developed in the mesentery, in the abdominal wall and in the superior mediastinum, these grossly suggested sarcoma formation One of these firm, nodular masses was attached to the mesentery by a short pedicle and was large enough to distend the abdomen considerably Microscopically, these tumors are really a giant collection of thick-capsulated organisms suspended in a fibrous network In animals showing such tumors, the infection appeared to have been successfully localized, since invasion of other organs could not be demonstrated Humoral antibodies were not demonstrable in the serums of these animals, nor in

8 Voyles and Beck [1a] Rappaport, B Z, and Kaplan, B Generalized Torula Mycosis, Arch Path **1** 720-741 (May) 1926 Crone, J T, DeGroat, A F, and Wahlin, J G Torula Infection, Am J Path **13** 863-879, 1937

(f) The parents were carefully instructed to watch for any of the aforementioned symptoms and to call as soon as a reaction was noted

REACTIONS IN NON-NERVOUS CHILDREN

The first four groups consisted of quiet, cooperative children, a fact that as far as possible eliminated nervousness as a cause of reaction

GROUP 1 This group consisted of 55 patients treated by means of a mechanically rectified National Wappler x-ray unit using an open General Electric Universal tube This tube had an inherent filtration of 0 5 mm of aluminum The voltage used was 80 kilovolts with no added filtration

In this group 5 patients had mild reactions, a percentage of 9 1

GROUP 2 This group consisted of 124 patients treated by means of a General Electric X-Ray KX 10 intermediate therapy unit with an SP 140 tube This tube had an inherent filtration of 1 0 mm of aluminum The voltage used was 100 kilovolts with no added filtration The half value layer was 1 4 mm of aluminum

Ninety-six patients had reactions They varied from mild to severe The severe reactions were extremely alarming However, at no time were there any convulsions The percentage of reactions in this group was 77 1 The earliest reaction occurred within fifty minutes and the latest fourteen hours after treatment

GROUP 3 This group consisted of 42 patients, who were treated by means of the same SP 140 tube, but with 80 kilovolts being used, and no added filtration The quality of irradiation was a half value layer of 1 1 mm of aluminum

In this group 12 patients had reactions, none of which were severe The percentage of reactions was 28 5

GROUP 4 This group consisted of 36 patients treated by means of the same SP 140 tube, 60 kilovolts being used, with no added filtration The quality of irradiation was a half value layer of 1 0 mm of aluminum

Five patients had reactions, none of which were severe The percentage of reactions was 13 9

REACTIONS IN NERVOUS CHILDREN

The next three groups consisted of nervous and restless patients This was arranged so that it might be determined whether nervousness could be a cause of increased reactions

GROUP 5.—This group consisted of 28 patients treated by means of the open General Electric Universal tube The voltage used was 80 kilovolts with no added filtration

Eighteen patients had reactions varying from mild to moderately severe The percentage of reactions was 64 3

PATHOLOGIC STUDIES EMPLOYING THE CHICK EMBRYO

The chorioallantoic membrane supports the growth of various pathogenic fungi [13] Moore showed that torula cells will grow on the surface of the membrane but was unable to demonstrate that the tissue was actually invaded We repeated Moore's work preliminary to determining whether or not the infected chick embryo could be used as a test object for chemotherapeutic studies

Inoculations were made by various routes The technic used for exposing the membrane was that of Lee and associates [14] A half cubic centimeter of a dense suspension of torula cells was dropped onto the exposed membrane of a 10 day old chick embryo After the membrane had been incubated for nine days at 37 C (Moore's observations were made after five days), gross inspection revealed a whitish material unevenly covering the membrane This proved to be a mass of torula cells The membrane itself did not appear to be materially altered On histologic section, the most characteristic feature observed was the presence of torula cells embedded within the thin ectodermal layer There was no proliferation of the ectodermal cells nor any infiltration of inflammatory cells around the torula organisms The ectodermal cells in some areas were hugely swollen, the picture being suggestive of hydropic degeneration A conspicuous and significant finding was the presence of buds on a great number of cells, which indicated that the cells were proliferating

A varying degree of polymorphonuclear infiltration occurred in the mesoderm, despite the fact that no free torula cells were present in this situation Very commonly, however, torula cells were seen within the lumens of the mesodermal capillaries Granulomas or abscesses were not formed No giant cells or lymphocytes were found The chick embryo response is thus strikingly different from that of other animal tissues Surface inoculation of the membrane commonly did not kill the embryos

Living cells were injected into the 10 day chick embryo intra-allantoically, intravenously, intra-amniotically and into the yolk sac The mortality resulting from the trauma of intravenous injection of saline solution alone was about 50 to 70 per cent, as compared with the 25 per cent mortality observed by Lee and associates [14] Embryos were given intravenous injections of 0 03 cc of a torula suspension containing 20,000,000 cells per cubic centimeter

13 Moore, M The Chorio-Allantoic Membrane of the Developing Chick Embryo as a Medium for the Cultivation and Histopathologic Study of Pathogenic Fungi, Am J Path **17** 103-120, 1941

14 Lee, H F , Stavitsky, A B , and Lee, M P A Chick Embryo Technique for Intravenous and Chemotherapeutic Studies, Proc Soc Exper Biol & Med **61** 143-149, 1946

The higher voltages and filtrations also increased the percentage and severity of the reactions

CONCLUSION

In cases of ringworm of the scalp in which roentgen ray epilation is indicated, low voltage not to exceed 80 kilovolts and low filtration not to exceed a half value layer of 0 5 mm of aluminum should be used These factors plus a quiet, cooperative child who has had a small quantity of food to eat will tend to lessen this variety of irradiation sickness without sacrificing a satisfactory therapeutic result

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the tissue to the fungicide was frequently so severe as to exclude this procedure as a useful test

THERMAL SENSITIVITY OF TORULA CELLS

While we were attempting to infect rabbits with torulosis, it occurred to us that their unusual resistance might be due to their high body temperature Following the intravenous injection of 100,000,000 torula cells, the normal rectal temperature of about 103 F rose to as high as 105 to 106 F for a period of about a week Studies of the thermal death point were accordingly undertaken with a view toward evaluating the possibility of fever therapy After our studies were complete, we discovered that Kuhn [16] had already reported on the subject When his cultures were exposed to temperatures of 105 and 107 F, the cells were killed in seven and in six days, respectively

Four different strains of cryptococcus were used in our study Three of these had been isolated from human beings with torulosis in the last two years, and all had had at least one recent passage through mice The fourth strain had been in stock culture for many years and was also virulent for mice

A preliminary study showed that all four strains reacted similarly to heat, being killed in ten minutes at 50 C and in three minutes at 70 C Next, temperatures were employed which fell within the range obtainable by artificially induced fever Tubes containing 5 cc of asparagine-glucose broth were inoculated with 0 2 cc of a one week broth culture of C neoformans They were then immersed in a thermoregulated, mechanically agitated water bath Each day thereafter 0 1 cc of the medium was pipetted into a tube of potato-dextrose agar (Difco) and incubated

The results are shown in table 2 It may be seen that at 40 C (104 F) all four strains were killed in six days This temperature is also the lowest one at which complete inhibition of growth occurred, although there was partial inhibition at 39 C (102 2 F) At 41 C (105 8 F), only four days were required for complete sterilization In respect to human fever therapy, the feasibility of a patient's tolerating a continuous temperature of 41 C for four days is indeed questionable, nonetheless the potential benefit of fever therapy, even if these requirements cannot be met, is not immediately excluded It must be appreciated that the thermal death points recorded previously are those required to kill 100 per cent of the cells An "endpoint" experiment of this kind reveals no information on the distribution of individual thermal susceptibilities of the cells comprising the population in the test tube

16 Kuhn, L R Growth and Viability of Cryptococcus Hominis at Mouse and Rabbit Body Temperatures, Proc Soc Exper Biol & Med **41** 573-574, 1939

longest period recorded having been seven years and eight months [4] Therapeutic efforts have included administration of iodides, sulfonamide compounds, vaccines, penicillin, acriflavine compounds, sodium thiosulfate, gold and sodium thiosulfate N F, colloidal copper and silver, immune (?) serum, merbromin (mercurochrome®), antimony and potassium tartrate (tartar emetic), mercury salts, methylrosaniline chloride (gentian violet) and alcohol intravenously, as well as roentgen irradiation and surgical procedures, among other forms of treatment This impressive list testifies to the futility of available therapeutic measures Incidentally, treatment is also inadequate in other progressive systemic mycoses, such as histoplasmosis, coccidioidomycosis and perhaps blastomycosis, fatal outcomes are commonplace in the disseminated forms of these diseases

The therapy of actinomycosis and nocardiosis by means of sulfonamide drugs and penicillin shows promise,[5] and the curative effect of iodides on sporotrichosis is a bright spot for the deficient armamentarium of the medical mycologist [6]

The studies reported here are necessarily diverse because the factors which could enable a rational approach to the therapy of torulosis are also diverse

PATHOLOGIC STUDIES

In man, the symptoms resulting from involvement of the central nervous system constitute the dominant aspect of the disease, nonetheless, systemic involvement is the rule, with widespread invasion of many organs [1a] Thus, Wade and Stevenson's experiments with mice inoculated by various routes indicated that, in addition to cerebral invasion, one can regularly produce lesions in the lungs and the kidneys and, less consistently, in the liver and the spleen [7] The following experiment was designed to follow up this work and, in addition, to provide an idea of how regularly organisms could be isolated from the blood stream

Twelve mice were each given intraperitoneal injections, and an equal number of intravenous ones, of 8,000,000 organisms The results are shown in table 1 Interestingly, the lungs were more frequently

4 Reeves, D L, Butt, E M, and Hammack, R W Torula Infection of the Lungs and the Central Nervous System Report of Six Cases with Three Autopsies, Arch Int Med **68** 57-79 (July) 1941

5 Keeney, E L, Libero, A, and Lankford, E Studies on Common Pathogenic Fungi and on Actinomyces Bovis II In Vitro Effect of Sulfonamides, Bull Johns Hopkins Hosp **75** 393-409, 1944

6 Conant, N F, and others Manual of Clinical Mycology, National Research Council, Division of Medical Sciences, Philadelphia, W B Saunders Company, 1944

7 Wade, L I, and Stevenson, L D Torula Infection, Yale J Biol & Med **13** 467-476, 1941

at high temperatures the amount of drug required to give inhibition is considerably less [18] Stokes,[19] in reviewing Eagle's work with syphilitic rabbits treated with combined fever and penicillin, reported that the curative effect of penicillin was increased eightfold by the fever In view of the practically hopeless prognosis in torulosis, one cannot ignore any lead, no matter how inconclusive [19a] The essential fact is that torula cells are definitely inhibited at the relatively low temperature of 40 C and are killed after six days at this temperature Moreover, the majority of cells are killed before this time Although fever therapy based on these data would be extreme indeed, the consequences of therapeutic inactivity are worse, and it is our judgment that fever therapy should be tested under careful supervision Torula cells in vivo may have a thermal sensitivity different from that exhibited by cells in vitro, moreover, if an inhibitory temperature can be maintained for a few days, the normal body defenses may rally to limit the course of the infection The best method of inducing fever in this particular situation is of course entirely speculative Perhaps malarial fever should be tried first

It is significant in this connection that fever is not a common symptom in human torulosis It is also to be recalled that spontaneous remissions do occur, which fact suggests that the body has some mechanism for dealing, albeit ineffectually, with the infection Fever therapy may augment this vague reaction Again, it is well to keep in mind the improved activity of chemotherapeutic drugs at high temperatures, so that any nontoxic drug showing fungistasis in vitro should be combined with fever therapy before being discarded as valueless

STUDIES OF FUNGISTATIC CHEMICALS IN VITRO

The method used was essentially a modification of the paper disk method employed in antibiotic testing Briefly, it consists of suspending torula cells in an agar medium and of measuring the zone of inhibition around impregnated paper disks placed on the surface of the medium The technic has been described elsewhere [20]

Fatty Acids and Derivatives Today, the fatty acids appear to be the drugs of choice in the treatment of the superficial mycoses [21] The

18 McCulloch, E C Disinfection and Sterilization, ed 2, Philadelphia, Lea & Febiger, 1945

19 Stokes, J H Recent Advances in Syphilologic Diagnosis and Treatment, Pennsylvania M J **50** 718-725, 1947

19a In a preliminary experiment which was subsequently done with intravenously inoculated chick embryos, there was clearcut evidence of protection when the embryos were incubated at 40 C instead of 37 C

20 Kligman, A M, and Rosenzweig, W A Simple Quantitative Method for the Laboratory Assay of Fungicides, J Invest Dermat **10** 51-58, 1948

21 Sulzberger, M B, and Kanof, A Undecylenic and Propionic Acids in the Prevention and Treatment of Dermatophytosis, Arch Dermat & Syph **55** 391-395 (March) 1947

those of any of the other rats Very rarely the infection in human beings localizes as a circumscribed lesion amenable to surgery[9] Evidently some vague defense reaction, of which we know little, exists.

Association of Leukosis The association of Hodgkin's disease with torulosis is too frequent to be ascribed to chance Lymphoblastoma has been conservatively estimated to occur in 5 to 10 per cent of the cases of torulosis[1b] The diagnosis of lymphatic leukemia was made in 1 instance[10] Generally the lymphoblastoma is discovered by biopsy prior to the diagnosis of torulosis, and the feeling seems to have been that the torulosis complicated a preexisting lymphoblastoma Fitchett and Weidman,[11] however, appeared to regard the condition in their case as being primarily torulosis, complicated by Hodgkin's disease In theorizing about this situation, Cox and Tolhurst[1b] suggested that the Hodgkin reaction may be provoked by some substance liberated by the organism, possibly a "carcinogenic-like" material present in the capsule Inasmuch as we had isolated the capsular material and identified it as a polysaccharide,[12] we undertook in a preliminary way to investigate its capacity to induce a lymphadenoid reaction in mice.

Four mice were given fourteen daily intraperitoneal injections consisting of 1 cc of a 2 per cent solution of the capsular substance In spite of this enormous dosage, no toxic reactions were observed and, in fact, 1 of the mice became pregnant and successfully carried to term At necropsy, the only significant gross finding was a moderate enlargement of the superior mediastinal lymph nodes, the histologic sections showed benign hyperplasia An interesting finding in the spleens of 2 of the mice was the presence of enlarged malpighian corpuscles, with diffuse infiltration of lymphocytes into the red pulp No abnormal cells were seen, however

This modest experiment, in our judgment, demonstrated a selective reaction on the part of the lymphatic system, but the reaction was certainly not characteristic of a lymphoblastomous process[12a]

9 Marshall and Teed[3a] Brewer, G E, and Wood, F C Blastomycosis of the Spine Double Lesion, Two Operations, Recovery, Ann Surg **48** 889-896, 1908

10 Magruder, R G A Report of Three Cases of Torula Infection of the Central Nervous System, J Lab & Clin Med **24**.495-499, 1939

11 Fitchett, M S, and Weidman, F D Generalized Torulosis Associated with Hodgkin's Disease, Arch Path **18**·225-244 (Aug) 1934

12 Kligman, A M Studies of the Capsular Substance of Torula Histolytica and the Immunologic Properties of Torula Cells, J Immunol **57** 395-401, 1947

12a Since this paper was submitted for publication, it has been shown that the capsule of C neoformans is dissolved by hyaluronidase, a finding which presumptively identifies the capsular material as hyaluronic acid This observation would explain the lack of antigenicity of the capsular material (Drouhet, E, and Segretain, G The Action of Hyaluronidase on the Capsule of T Histolytica, Compt rend Acad d Sc **228**·424-425, 1949)

Sulfonamide Compounds—None of the sulfonamide compounds showed any inhibitory effect in a concentration of 1 400 The compounds tested were sulfamerazine, sulfadiazine, sulfanilamido-acetic acid, sulfathiazole, sulfanilamide, sodium-5-sulfanilamido-napthalene-1-sulfonate, sodium sulfanilyl-sulfanilate, sodium-2-sulfanilamido benzoate, 4-allylamino-4′-amino-diphenyl-sulfone, 3′,5′-dibromosulfanilanilide, N^1-*p*-nitrobenzoyl sulfanilamide, silver mercaptoacetyl sulfathiazole and sodium bismuth mercaptoacetyl sulfathiazole

TABLE 4—*Fungistatic Activity of Naphthoquinones and Related Compounds (Millimeters of Inhibition)*

Compound *	Pennsylvania Medium ‖				20 per Cent Blood Medium ¶			
	1 1,000	1 5,000	1 10,000	1 50,000	1 1,000	1 5,000	1 10 000	1 50,000
5-Hydroxy 1,4 naphthoquinone	22	18	16	15	20	16	14	0
2 Chloro 1,4 naphthoquinone	33	23	20	18	18	17	0	0
2,3 Dichloro 1,4 naphthoquinone	27	25	23	19	17	14	0	0
2,3 Dichloro 5-hydroxy 1,4 naphthoquinone	24	18	16	15	24	20	15	0
2 Chloro 3 dimethylamino 1,4 naphthoquinone	33	20	18	15	26	14	0	0
2 Chloro 3 (*p* tolylthioxy) 1,4 naphthoquinone	21	18	12	0	0	0	0	0
2 Thiocyano 3 chloro 1,4 naphthoquinone	23	20	18	17	19	17	14	0
2 Methyl 1,4 naphthoquinone†	40	38	20	11	35	26	0	0
2 Methyl 1,4 naphthoquinone 3 sodium sulfonate‡	0	0	0	0	0	0	0	0
Tetrasodium diphosphoric ester of 2 methyl 1,4 naphthoquinone§	0	0	0	0	0	0	0	0
2 Methoxy 3 chloro 1,4 naphthoquinone	25	18	17	0	18	0	0	0
2 (o Chloromercuriphenoxy) 3 chloro 1,4 naphthoquinone	34	27	18	16	17	0	0	0
2 (p Chlorophenoxy) 3 chloro 1,4 naphthoquinone	28	22	17	0	21	16	0	0
Tetrachloro benzoquinone	18	17	15	13	0	0	0	0
Tetrachloro hydroquinone	25	20	0	0	0	0	0	0
2,2 3,4,4 Pentachloro 1 keto tetrahydro naphthalene	30	25	18	15	0	0	0	0
Phenanthraquinone 9,10	45	43	25	17	19	15	0	0

* All compounds not otherwise credited were secured through Dr G L McNew, United States Rubber Company, Naugatuck, Conn

† Menadione U S P ("Thyloquinone" Squibb)

‡ Vitamin K preparation (Abbott Laboratories, Inc)

§ Vitamin K preparation (Hoffmann LaRoche)

‖ Pennsylvania medium is prepared of 40 Gm of crude dextrose, 10 Gm of peptone, 20 Gm of agar and 1 liter of water

¶ The blood medium is prepared by the addition of 20 cc of horse blood to 80 cc of Pennsylvania medium

Napthoquinones and Related Compounds—Ter Horst[23] reported the high fungistatic properties of 2,3-dichloro-1,4-napthoquinone against a number of saprophytic fungi Our results with certain napthoquinones against various pathogenic fungi have been reported

23 ter Horst, W P, and Felix, E L 2, 3-Dichloro-1, 4-Napthoquinone A Potent Organic Fungicide, Indust & Engin Chem (Indust Ed) **35** 1255-1258, 1943

When the inoculation was made intra-amniotically or intra-allantoically, the dose was 0 3 cc of the same suspension With the latter routes infection of the embryo failed repeatedly After an unsuccessful attempt to establish infection with intravenous inoculation of a stock strain, a strain was isolated from a patient with torulosis, with which strain infection could be easily accomplished Subsequently, other stock strains proved suitable Within one week after intravenous infection enormous numbers of organisms could be seen in the kidney, spleen, brain, lungs and liver The histopathologic reaction was minimal and in this regard the effects resembled human lesions The mortality rate, exclusive of that occurring within the first forty-eight hours, depends on the size of the inoculum This can be arranged so as to produce 100 per cent mortality within nine days When fewer cells are injected, most of the animals survive, so that cultural or histopathologic examinations are required in order for one to demonstrate the infection We have found that the mortality which occurs from trauma is somewhat reduced when 9 day old instead of 11 day old embryos are used

It would appear, then, that the intravenous inoculation of chick embryos with C neoformans is a technic which may have promise in the evaluation of chemotherapeutic agents A compromising difficulty with intravenous injections is the sizable mortality, which varies from week to week This can be overcome by the use of a larger number of eggs and the exclusion of the embryos which die within forty-eight hours, since the latter deaths probably result from trauma

STUDIES WITH THE RABBIT EYE

After beginning this work we became aware that Weiss and his co-workers [15] had already reported on the histopathologic response following the injection of torula cells into the anterior chamber of the rabbit eye Our findings corroborate theirs The most striking feature is the picturesque rosette which forms in the fibrinous exudate This is composed of a single torula cell surrounded by a ring of eosinophils and polymorphonuclear leukocytes No invasion of the cornea, iris or lens occurred

Subsequently we simultaneously inoculated the anterior chamber with torula cells and various fungistatic agents Although we could in some instances prevent infection with this technic, the reaction of

15 Weiss, C , Perry, I H , and Shevky, M C Infection of the Human Eye with Cryptococcus Neoformans (Torula Histolytica, Cryptococcus Hominis) A Clinical and Experimental Study with a New Diagnostic Method, Arch Ophth 39 739-751 (June) 1948

and one may suspect that this particular fraction is lost during the commercial extraction of penicillin

Antibiotics having an appreciable effect on C neoformans are listed in table 5 The most effective were allicin, pleurotin, bacillomycin B and actidione The last is especially interesting since it has an almost specific fungistatic action on C neoformans, not being nearly as active against other pathogenic fungi The table shows clearly that C neoformans is extremely susceptible to several antibiotics and exhibits no singular resistance

Thiocarbamate Derivatives Urethane (ethyl carbamate), a drug which has shown some promise in the treatment of the lymphoblastomas,

TABLE 5.—*Fungistatic Effect of Certain Antibiotics (Millimeters of Inhibition)*

Antibiotic	1 1,000	1 2,000	1 5,000	1 10,000	1 50,000	1 100,000
Actidione *	57		48	42	37	21
Allicin †	51	45	35	33	26	22
Pleurotin ‡	44	27	25	19	17	14
Bacillomycin B §	40	38	36	34	28	0
Biformin ‡	28	26	25	18	0	0
Protoanemonin ‖	35	32	19	17	0	0
Gliotoxin	38	32	25	0	0	0
Lavendulin ¶	22	20	17	0	0	0
Streptothricin	22	20	0	0	0	0
Actinorubin ¶	22	19	0	0	0	0
Viridin #	25	16	0	0	0	0
Citrinin	19	0	0	0	0	0

* Secured from Dr A J Whiffen, Upjohn Company, Kalamazoo, Mich
† Secured from Sterling Winthrop Research Institute, Rensselaer N, Y
‡ Secured from Dr William J Robbins, New York Botanical Garden, New York
§ Secured from Dr G H Warren, John Wyeth Institute, Philadelphia
‖ Secured from Dr Beatrice Seegal, Columbia University College of Physicians and Surgeons, New York
¶ Secured from Dr Harry E Morton, Department of Bacteriology, University of Pennsylvania Medical School, Philadelphia
\# Secured from Imperial Chemical Industries Limited, London, England

belongs to a group of compounds which are already in use as fungicides for the control of plant diseases [31] Our results are shown in table 6 Some of these drugs have pronounced fungistatic activity which is maintained in the presence of whole blood They are by far the most active of the synthetic materials which we have investigated Their activity against other fungus pathogens has been reported elsewhere [24]

Miscellaneous Compounds Several hundred miscellaneous compounds were tested, none of which were effective in the initial dilution of 1 500 The following list is a partial one and indicates the range of

31 Richards, M C The Control of Alternaria Blight on N H Victor Tomatoes by the Application of Fungicides, Phytopath **35** 656-657, 1945 Heuberger, J W, and Manns, T F New Organic Fungicides in the Control of Tomato and Potato Diseases, ibid **35** 485, 1945

In other words, it is not to be expected that every cell would require exposure to exactly the same temperature for death

To investigate this point we made up suspensions of cells as previously described and placed them in the water bath at 104 F (40 C) At twenty-four hour intervals, a cell count was made by the plate dilution method and performed in triplicate The initial count was 250,000 cells per cubic centimeter At the end of twenty-four hours this had fallen to 76,000, or, in other words, almost three quarters of the cells were killed in one day On the second day 13,700 viable cells remained The number decreased steadily, so that 800 living cells were left on the fourth day and 600 on the fifth day The essential observation in this experiment is that the majority of the cells were killed in one day

TABLE 2—*Inhibiting and Lethal Temperatures for Four Strains of Cryptococcus Neoformans*

Strain of Cryptococcus	Temperature (C)	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8	
		A*	B†	A	B	A	B	A	B	A	B	A	B	A	B	A	B
T	39	0	+	0	+	0	+	—	+	—	+	—	+	—	+	+	+
A		0	+	0	+	0	+	—	+	—	+	—	+	—	+	—	+
M 89		0	+	0	+	0	+	—	+	—	+	—	+	—	+	—	+
M 30		0	+	0	+	0	+	—	+	—	+	—	+	—	+	+	+
T	40	0	+	0	+	0	+	—	+	—	+	—	—	—	—	—	—
A		0	+	0	+	0	+	—	+	—	+	—	—	—	—	—	—
M 89		0	+	0	+	0	+	—	+	—	—	—	—	—	—	—	—
M 30		0	+	0	+	0	+	—	+	—	+	—	—	—	—	—	—
T	41	0	+	0	+	0	+	—	—	—	—	—	—	—	—	—	—
A		0	+	0	+	0	+	—	—	—	—	—	—	—	—	—	—
M 89		0	+	0	+	0	+	—	—	—	—	—	—	—	—	—	—
M 30		0	+	0	+	0	+	—	—	—	—	—	—	—	—	—	—
T	42	0	+	0	+	0	+	—	—	—	—	—	—	—	—	—	—
A		0	+	0	+	0	—	—	—	—	—	—	—	—	—	—	—
M 89		0	+	0	+	0	—	—	—	—	—	—	—	—	—	—	—
M 30		0	+	0	+	0	—	—	—	—	—	—	—	—	—	—	—
Control	37	0	+	0	+	0	+	+	+	+	+	+	+	+	+	+	+

* Column A indicates macroscopic growth in culture (no observable growth in control until fourth day)
† Column B for each day indicates growth as determined by subculture

In view of the prolonged high temperature required to effect sterilization, intermittent exposures were given at 40 C for eight hours each day for eight consecutive days At the end of this time, viable cells were still present Unfortunately, cell counts were not made It is doubtful that fever therapy alone holds promise in the treatment of torulosis, however, one cannot decisively dismiss it as an adjuvant until it has been tried clinically [17] It is well known that the efficacy of chemotherapeutic agents increases directly as the temperature does, so that

17 Of interest in this regard is the report (personal communication to the authors) of a patient in an Army hospital who was simultaneously ill with malaria and torulosis It was observed that relapse with respect to the malaria, with chills and fever, was accompanied with improvement of the torulosis symptoms and by disappearance of the organisms from the spinal fluid Unfortunately, a follow-up is not available This occurrence may, of course, have been simply coincidental The patient was also given quinacrine (atabrine®)

Quinone Derivatives—No protection was afforded by any of these derivatives (table 7) This result was in agreement with the finding that the fungistatic action of this group is reversed by whole blood in vitro

Carbamate Derivatives These compounds were promising in view of their high fungistatic potency and low toxicity for mice The results were entirely disappointing (table 8) The dosage was varied in

TABLE 7—*Effects of Quinone Derivatives in Vivo, with Intraperitoneal Injection of 4,000,000 Torula Cells*

	Dosage, Mg /kg	Median Lethal Dose, Mg /kg	Days of Survival								Average Days of Survival
2 Chloro 3 dimethylamino 1,4 naphtho quinone	50	70	11	14	14	17	26	30	32		21
2,2,3,4,4 Pentachloro 1 keto tetra hydronaphthalene	50	75	6	6	9	11	12	21	38		15
2 Th ocyano 3 chloro 1,4 naphtho quinone	50	75	14	17	17	28	29				21
Tetrachloro benzoquinone	100	170	8	15	16	19	23	30	30		20
Phenanthraquinone 9,10	100	165	5	8	11	13	18	18	19	21	14
Control (4,000,000 torula cells)			6	9	13	13	20	27	34		17

TABLE 8—*Effect of Carbamate Derivatives in Vivo, with Intraperitoneal Injection of 4,000,000 Torula Cells*

	Dosage, Mg /Kg	Median Lethal Dose, Mg /kg	Days of Survival								Average Days of Survival
Sodium dimethyldithiocarbamate	400	560	12	19	21	21	32	33	38	38	27
Calcium dimethyldithiocarbamate	400	630	5	8	9	12	14	14	18	21	13
Ferric dimethyldithiocarbamate	200	315	6	6	8	11	31	40			17
Disodium ethylene bisdithiocarbamate	400	580	7	13	16	17	28	32			19
Control (4,000,000 torula cells)			6	9	13	13	20	27	24		17

different manners and included daily administration for seven days, but no protective effect could be demonstrated

Antibiotics The pronounced efficacy in vitro of some of these substances, particularly actidione, led us to approach therapeutic trials with real enthusiasm The actual results were uniformly unpromising (table 9)

Actidione was further investigated, as follows (1) A daily dose of 25 mg per kilogram was given for five days, and (2) two doses of 50 mg per kilogram were given, with an interval of twelve hours No protection was afforded Actidione is not inactivated by whole blood, and there is no obvious explanation for the failure of this drug

fungistatic activity increases with the length of the carbon chain, reaching a maximum at about C_9 and falling off again after C_{13} [22] Rothman and associates [22b] succeeded in demonstrating that the principal fungistatic components of human hair fat are the fatty acids C_7, C_9, C_{11}, C_{13} (heptylic, pelargonic, undecylenic and tridecanoic) We undertook to determine whether or not they held any promise for systemic use

The results are shown in table 3 In this series, pelargonic, capric and undecylenic acids were the most effective, but none had outstand-

TABLE 3.—*Fungistatic Effect of Fatty Acids and Their Salts (Millimeters of Inhibition)**

Compound	Dilution 1 100	1 500	1 1,000	1 2,000
Propionic acid	15	0	0	0
Sodium propionate	0	0	0	0
Valeric Acid	22	0	0	0
Sodium valerate	0	0	0	0
Caproic acid	26	0	0	0
Sodium caproate	0	0	0	0
Caprylic acid	41	35	0	0
Sodium caprylate	39	12	0	0
Pelargonic acid	43	35	25	14
Sodium pelargonate	45	31	24	0
Capric acid	40	36	25	19
Sodium caprate	43	30	18	16
Undecylenic acid	40	32	23	14
Sodium undecylenate	38	29	18	0
Cyclohexyl acetic acid	0	0	0	0
Sodium salt	0	0	0	0
Cyclohexyl propionic acid	30	22	17	0
Sodium salt	24	0	0	0
Cyclohexyl butyric acid	35	31	20	0
Sodium salt	24	0	0	0
Cyclohexyl caproic acid	20	17	17	0
Sodium salt	23	17	17	0
Propionyl salicylic acid	0	0	0	0
Sodium salt	0	0	0	0
Cyclohexyl valeric acid	0	0	0	0
p Phenylcyclohexyl acetic acid	0	0	0	0
Beta 2 Tetraloylpropionic acid	0	0	0	0

* Most of the acids were supplied by the Mycoloid Laboratories, Little Falls, N J The sodium salts were adjusted to p_H 7 0

ing fungistatic potency The sodium salts were less effective than the corresponding acids, a phenomenon already known to be a property of this group Unfortunately, whole blood, added to the medium, antagonized the fungistatic activity

22 (*a*) Keeney, E L , Libero, A , and Lankford, E Studies on Common Pathogenic Fungi and Actinomyces Bovis I In Vitro Effect of Fatty Acids, Bull Johns Hopkins Hosp **75** 377-392, 1944 (*b*) Rothman, S , Smiljanic, A , Shapiro, A L , and Weitkamp, A W The Spontaneous Cure of Tinea Capitis in Puberty, J Invest Dermat **8** 81-97, 1947

SUPERFICIAL MYCOSES OF VETERANS

I Survey of One Thousand Veterans with a Service Diagnosis of Dermatomycosis

R C BURKE, Ph D
CAMBRIDGE, MASS
AND
F E BUMGARNER, M D
LOS ANGELES

IT WAS BELIEVED by many that a number of new strains, and possibly new species, of pathogenic fungi would be found in soldiers returning from the tropics, but the course of the war brought no reports of infections with new organisms or of rare infections, such as tinea imbricata, infrequently found in this country However, such colloquialisms as "jungle rot," "New Guinea rot" and "swamp rot" were applied to cutaneous diseases in the tropics, terms used not only by the soldiers but even creeping into diagnostic slips of medical officers The discovery of a mycelium in some of the lesions familiarly termed "jungle rot" led many persons to believe that most of these conditions were mycotic in origin

A review of service medical records of World War II, of both the Army and the Navy, has been possible during the past two years The well known penchant for designating lesions of the feet and hands as due to fungi has been amply demonstrated This review has adequately, even painfully, revealed that the cooperation of dermatologically trained clinicians and technicians skilled in mycology might have prevented many erroneous concepts concepts now evident in the great number of claims and pensions for service-incurred or service-aggravated cutaneous diseases The superficial mycoses, or those so termed in the services, head the long list

During the two year period between December 1945 and December 1947, 1,000 veterans with service diagnoses of superficial mycoses were examined at the Los Angeles Veterans Administration outpatient dermatology clinic and mycology laboratory These patients came from various areas of troop distribution throughout the world, chiefly the Southwest Pacific No patient who had been separated from the

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elsewhere [24] Wooley [25] was able to bring about reversal of the fungistatic effect by means of synthetic vitamin K Our results with a series of quinone derivatives are shown in table 4 Although many compounds in this group show strong activity in vitro, the presence of whole blood in the medium seriously reduces this activity Of considerable interest is the pronounced fungistatic activity of one of the synthetic vitamin K's, menadione U S P (2-methyl-1,4-napthoquinone) Some of the members of this group were selected for further study, and the results are given later in this paper

Antibiotics In connection with the search for new antibiotics which is being vigorously pursued by many investigators, some drugs have emerged which appear to have antifungal properties Those active, in vitro, against certain strains of C neoformans are tomatin,[26] actidione,[27] bacillomycin B [28] and eumycin [29]

The following antibiotics were found by our method to be inactive against our strains of C neoformans tyrothricin, crude penicillin, penicillin G, penicillin K, streptomycin, penicillic acid, tyrocidin, gramicidin, subtilin, bacitracin, gladiolic acid, glutinosin, crepin, kojic acid and aspergillic acid [29a] The relatively crude sample of tomatin that we employed exhibited no fungistasis in vitro Fontaine,[26] however, reported that tomatin was inhibitory in a concentration of 1 unit per cubic centimeter Hobby and associates [30] reported the presence of an antitorula substance in the filtrate of cultures of Penicillium notatum,

24 Kligman, A M, and Rosenzweig, W Studies with New Fungistatic Agents I For the Treatment of Superficial Mycoses, J Invest Dermat **10**. 59-68, 1948

25 Wooley, D W Observations on Antimicrobial Action of 2,3-Dichloro-1, 4-Napthoquinone and Its Reversal by Vitamin K, Proc Soc Exper Biol & Med **60**· 225-228, 1945

26 Fontaine, T D, Irving, G W, and Doolittle, S P Partial Purification and Properties of Tomatin an Antibiotic Agent from the Tomato Plant, Arch Biochem **12** 395-398, 1947

27 Whiffen, A J, Bohonos, N, and Emerson, R L The Production of an Antifungal Antibiotic by Streptomyces Griseus, J Bact **52** 610-611, 1947

28 Landy, M, Rosenman, S B, and Warren, G H An Antibiotic from Bacillus Subtilis Active Against Pathogenic Fungi, abstracted, J Bact **54** 24, 1947

29 Burdon, K L, and Johnson, E A Progress Report on Eumycin, read before the Conference on Antibiotic Research, National Institute of Health, Washington, D C, Jan 31, 1947

29a Subsequently chloramphenicol (chloromycetin®), aureomycin and lupulon were found to be ineffective Polymyxin was inhibitory in a dilution of 1 1,000 but not in one of 1 5,000

30 Hobby, G L, Meyer, K, and Chaffee, E Activity of Penicillin in Vitro, Proc Soc Exper Biol & Med **50** 277-280, 1942

A diagnosis of tinea manus was recorded for 255 patients, for only 48 of whom laboratory results were positive (1 4 3) The majority of the negative results were obtained from vesicular exudative lesions, particularly of the fingers The mycology laboratory has found all such lesions of the hands to be negative for fungi unless the vesicular eruption is an extension of a lesion of tinea corporis from the wrist and dorsum of the hand onto the fingers On the other hand, it has been found that the type of tinea manus most frequently overlooked is that of chronic hyperkeratotic scaling of the palm and the ventral surface of the fingers

TABLE 2—*Ratio of Positive to Negative Areas in Cases of Dermatophytosis and Cutaneous Moniliasis*

Area	Total Number Examined	Number of Positive Areas	Number of Negative Areas	Approximate Ratio
Feet	670	360	310	1 2 1
Nails of feet and hands	264	245	19	12 8 1*
Groin	130	86	44	2 1
Leg	62	15	47	1 3
Buttocks	31	20	11	2 1
Upper portion of trunk	40	10	30	1 3
Axilla	27	7	20	1 3
Arms	35	4	31	1 8
Scalp	10	4	6	2 3*
Abdomen	9	5	4	5 4
Neck	18	7	11	1 1 5
Perineum	27	2	25	1 12 5
Penis	5	0	5	
Scrotum	12	0	12	
Concha of ear	4	4	0	
Mouth	6	1	5	1 5
Face	15	1	14	1 14
Hand	255	48	206	1 4 3*
Total	1,619	819	800	1 1

* These ratios are misleading, since in many positive areas discovered in the clinic the infection had not been diagnosed earlier

Weidman and Glass[2] stated the belief that Negroes have dermatophytosis more frequently than have white persons The results of this study do not confirm that conclusion Approximately one third of the patients examined, and one third of the patients who were shown to have dermatophytosis, were Negroes We were able, however, to confirm the statement of Weidman and Glass that Trichophyton gypseum is isolated more frequently, and also that the "soft corn" intertriginous lesions are found oftener in Negroes than in white persons In fact, T gypseum was cultured in several cases of chronic

2 Weidman, E D, and Glass, F A Dermatophytosis and Other Forms of Intertriginous Dermatitis of the Feet, Arch Dermat & Syph 53 213 (March) 1946

compounds investigated propamidine, hyamine 1622, hyamine 10x, 6-phenyl-5,6-dihydrouracil, 3-phenyl hydantoin, 2-(dimethylaminomethyl)-1-naphthol hydrochloride, 4,4'-dihydroxy-3,3'di (diethylaminomethyl)-5,5'-diallyl-diphenyl dihydrochloride (these last two compounds are members of the group of Mannich reaction products, four more of which were tested), neoarsphenamine, antimony potassium tartrate, resorcinol, dichlorophenarsine, phenazine di-N-oxide, stibophen (fuadin®), nicotinamide, promizole® (4,2'-diaminophenyl-5'-thiazolylsulfone), promin® (sodium p,p'diaminodiphenylsulfone-N,N'-didextrose sulfonate), nitrofurazone (furacin®), diethylstilbestrol, *p*-nitrobenzoic acid, phenothiazine, *p*-aminobenzoic acid, *p*-aminohippuric acid, quinacrine (atabrine®), quinine, 6-methoxy-8-morpholino-propylamino quinoline, 6-methoxy-8-isopropyl-amino-pentylaminoquinoline, N-butylmaleimide, 6-cyano-2-methoxy-9-isopropylaminopropyl-aminoacridine (3

TABLE 6.—*Fungistatic Effect of Some Carbamate Derivatives (Millimeters of Inhibition)*

Compound	Pennsylvania Medium				20 per Cent Blood Medium			
	1 1,000	1 5,000	1 10,000	1 50,000	1 1,000	1 5,000	1 10,000	1 50,000
Disodium ethylene bisdithiocarbamate †	55	46	38	34	51	35	27	23
Calcium dimethyldithiocarbamate * (2)	51	38	35	22	20	28	22	18
Ferric dimethyldithiocarbamate * (3)	42	28	24	18	40	17	15	12
Zinc dimethyldithiocarbamate * (4)	38	33	20	18	28	18	15	12
Sodium dimethyldithiocarbamate * (1)	30	19	18	14	25	13	12	0
Urethane (ethyl carbamate)†	0	0	0	0	0	0	0	0

* Obtainable from E I du Pont de Nemours, Wilmington, Del
† Obtainable from Rohm and Haas Company, Philadelphia

other acridines also tested), 5-amino-7-hydroxy-1-triazole (d) pyrimidine and 2-metanilamido-5-chloropyrimidine

STUDIES IN VIVO

The median lethal doses were determined in mice according to the method of Reed and Muench[32] Arbitrarily, we considered compounds having a median lethal dose of 70 milligrams per kilogram or less too toxic for further study unless the fungistatic effect in vitro was extraordinary

Animal protection tests were conducted as follows Four million torula cells (counted in a hemocytometer) were injected intraperitoneally into white mice weighing 20 to 25 Gm , immediately the drugs, suspended in propylene glycol, were given by the same route Eight mice were used in the study of each drug

It was found that the range of survival varied considerably even in the control animals A number of animals failed to die within the observation period, and in one preliminary test fully 50 per cent of the control animals survived The utmost caution must be employed in interpreting results

32 Reed, L J , and Muench, H A Simple Method of Estimating Fifty Percent Endpoints, Am J Hyg **27** 493-499, 1938

Table 4 presents the incidence of the four species according to area rather than case A total of 369 positive cultures (45 per cent) were obtained from the 819 positive areas The total percentage of cultures of T gypseum decreased to 52 per cent, and that of cultures of T rubrum increased to 43 per cent This observation indicates that T rubrum causes generalized dermatophytosis oftener than does T gypseum Individual attention will be given to the various types of dermatophytosis in the second part of this paper

Tinea Versicolor —The incidence of tinea versicolor among white persons was the same as that among Negroes The 40 cases in which

TABLE 4—*Sources of Cultures in Cases of Dermatophytosis and Cutaneous Moniliasis*

Site	Positive Areas	No of Cultures	Percentage of Positive Cultures	Tinea Gypseum	Tinea Rubrum	E Floc cosum	Candida Albicans
Feet	360	186	51	118	58	4	6
Toe nails	222	74	33	45	29		
Groin	86	29	33	8	16	1	4
Hand	48	27	55	9	18		
Finger nails	23	13	56	6	7		
Buttocks	20	6	30	0	6		
Legs	15	6	50	2	4		
Upper part of trunk	10	4	40		4		
Abdomen	5	5	100	1	4		
Neck	7	5	70	1	4		
Scalp	4	2	50		2		
Face	1	1	100	1			
Axilla	7	4	57	1	3		
Arms	4	1	25		1		
Perineum	2	2	100				2
Mouth	1	1	100				1
Concha of ear	4	3	75	1	2		
Total	819	369	45	193	158	5	13
Percentage				52 3	42 8	1 4	3 5

Malassezia furfur was demonstrated, together with 7 additional cases, were presented in an earlier paper,[3] in which it was shown that approximately one fourth of the patients had lesions on the back of the neck and that most of these patients also had positive seborrhea-like lesions of the occipital region of the scalp

Erythrasma —One case of erythrasma was recorded, that of a Negro aged 29, who presented a well circumscribed lesion of the right axilla and a few punctate lesions of the upper portion of the right chest of eight months' duration He had concurrent tinea versicolor of the upper region of the trunk The erythrasma had not been diagnosed,

3 Bumgarner, F E, and Burke, R B Pityriasis Versicolor Atypical Clinical and Mycologic Variations, Arch Dermat & Syph **59** 192 (Feb) 1949

Miscellaneous Compounds The following substances failed to afford protection. (1) sodium pelargonate, 500 mg per kilogram; (2) sodium undecylenate, 400 mg per kilogram, (3) sodium caprate, 150 mg per kilogram, and (4) methylrosaniline chloride (methyl violet), 25 mg per kilogram

TABLE 9—*Effects of Antibiotics in Vivo, with Intraperitoneal Injection of 4,000,000 Torula Cells*

	Dosage, Mg /kg	Days of Survival								Average Days of Survival
Pleurotin	25	14	17	24	26					20
Allicin	100	9	14	14	18	23	34	35		21
Bacillomycin B	25	6	9	13	14	16	16	23	37	17
Protoanemonin	25	11	11	16	26	27	31	38		23
Actidione	100	9	10	14	20	20	27			20
Control (4,000,000 torula cells)		16	21	21	22	24	25	31		23

SUMMARY

In infected mice, inoculated either intravenously or intraperitoneally, C neoformans can commonly be isolated from the blood stream The lungs are invaded at least as frequently as the brain, and the generalized nature of the infection is obvious

Both the inhibiting and the lethal temperatures for the organism were determined The number of viable organisms decreased steadily at 40 C, with complete sterilization of a test tube population in six days The possibility of fever therapy for human torulosis is discussed

Of the fungistatic materials tested, the best results in vitro were secured with certain thiocarbamate derivatives and several antibiotics Animal protection studies with these agents revealed that they failed to prevent infection

Department of Dermatology & Syphilology, University of Pennsylvania School of Medicine

lesions on both feet, several toe nails and finger nails, the right palm and the concha and canal of the right ear All lesions were of the dry, chronic hyperkeratotic scaling type The concha of the right ear was erythematous, with fine hyperkeratotic scales The auditory canal also showed hyperkeratotic scaling, with evidence of maceration in the deeper portions T rubrum was isolated from lesions on the feet, the right hand and the right auditory canal

COMBINED, CONCURRENT AND CONSECUTIVE INFECTIONS

A total of 16 cases of combined, concurrent or consecutive infections were noted The 5 cases of combined involvement included 3 cases of infection of the plantar surfaces with T gypseum and T rubrum and 2 cases of involvement of intertriginous areas of the feet with T gypseum and C albicans There were 10 cases of concurrent involvement, the infections in 6 being due to T gypseum and M furfur, in 1 to E floccosum (feet) and T gypseum (toe nails) and in 1 to a combination of T gypseum and T rubrum (feet) and to T rubrum (groin) Only 1 case of possible consecutive infection was noted In this case C albicans had been cultured from intertriginous lesions of the feet in August 1946 In September 1947 the same intertriginous areas yielded T rubrum It is not improbable that T rubrum was present at the time C albicans was isolated and that the infection in this case was in reality a combined one

DERMATOPHYTID REACTIONS

In 29 cases, approximately 7 per cent of the total number of patients with dermatophytoses, there were exanthems interpreted by us as allergic In all but 1 of these cases this manifestation appeared in the form of a vesicular eruption of the hands, and occasionally of the feet In 1 case an erysipeloid-like lesion of the leg occurred each time bullous lesions appeared on the feet

In contrast to the 28 cases of eruptions of the hands interpreted by us as being dermatophytids, there were 48 cases of tinea manus In 38 of these there was concurrent involvement of the feet, and frequently of other areas as well This observation indicates that tinea pedis with dermatophytids of the hands occurs less frequently than does tinea pedis with tinea manus This does not agree with the opinion expressed by Pillsbury, Sulzberger and Livingood [4] However, we agree with these authors if only vesicular eruptions on the hands are considered It was found that the most frequent type of tinea manus was that of a chronic hyperkeratotic scaling of the palmar surface, rather than a vesicular eruption It was noted from the medical records of these veterans that almost any vesicular eruption was considered as tinea by the majority of medical officers

4 Pillsbury, D M , Sulzberger, M B , and Livingood, C S Manual of Dermatology, Philadelphia, W B Saunders Company, 1942

service for more than one year was included These ex-servicemen were from all walks of life and from all parts of the United States

A total of 1,731 cutaneous areas [1] were examined from these 1,000 patients Nine hundred and twenty-five patients, representing 1,619 areas, were examined for dermatophytosis, 41 patients, for otomycosis (aspergillosis of the ear), 40 patients (77 areas), for tinea versicolor, and 1 patient each, for erythrasma and black, hairy tongue For the 429 patients who were shown to have dermatophytosis and superficial moniliasis, there were 819 positive areas, an approximate average of 2 areas per patient The 496 patients who were shown not to have a dermatomycosis had a total of 800 negative areas In all, a total of 466 (46 6 per cent) of the patients were shown to have superficial mycoses by laboratory findings An approximate 10 per cent of the patients for whom laboratory findings were negative showed clinical evidence of dermatomycosis The 466 cases with positive laboratory findings were unevenly distributed among six types of superficial mycoses, with dermatophytosis comprising 87 1 per cent of the total (table 1) It should be noted that in table 1 the total of 476 includes 10 cases with 2 types of superficial mycoses

TABLE 1.—*Incidence of Superficial Mycoses*

	Number of Cases	Percentage of Cases
Dermatophytosis	416	87 1
Moniliasis	13	3 0
Tinea versicolor	40	8 4
Otomycosis	5	1 1
Erythrasma	1	0 2
Black tongue	1	0 2
Total	476	100 0

SUPERFICIAL MYCOSES

Dermatophytosis The 416 patients with dermatophytosis yielded a total of 806 positive areas tinea pedis ranked first in incidence, followed, in order, by tinea unguium, tinea cruris, tinea manus and generalized tinea The over-all ratio of positive to negative areas was 1 1 This figure is misleading, since there was great variation with regard to individual clinical areas (table 2) For instance, tinea cruris had a ratio of positive to negative areas of 2 1, tinea pedis, 1 1, lesions of the perineum, 1 12 5, and tinea of the arm, 1 8

1 Numerous sites may have been examined within one area—for example, dorsal and plantar sites of the foot area Tinea of both feet, of both hands or of the ears was counted as of one area

PYOSTOMATITIS VEGETANS

Report of Three Cases

FRANCIS P McCARTHY, M D
BOSTON

FROM the time of the original description of *pyodermatite végétante* by Hallopeau,[1] a small number of vegetating dermatoses have been described in the literature There has been considerable confusion in the reports of cases classified as dermatitis vegetans, especially in the American literature since the report by Hartzel[2] in 1901, when he first used the term Many cases not related to Hallopeau's *pyodermatite végétante* have been classified as dermatitis vegetans without conforming to the clinical and pathologic pictures seen in *pyodermatite végétante* of Hallopeau

In reporting 3 cases primarily involving the oral cavity, in 2 of which the condition remained an oral entity throughout the entire course of the disease and in the third of which a secondary cutaneous eruption developed a year after the primary oral condition, the name pyostomatitis vegetans is suggested as the one best suited to describe the disease The clinical appearance, the course and the pathologic picture in all 3 cases were essentially identical, and the vegetating skin condition in case 2 helped to clarify the diagnosis in these cases, as up to the complicating skin eruption no definite diagnosis of the oral lesions was made

The disease *pyodermatite végétante* (Hallopeau) is extremely rare, and most of the cases were reported in the two first decades of this century Hallopeau's descriptions of the first cases reported present a very complete clinical and histologic description of the cutaneous lesions The oral lesions clinically described in the original cases correspond to those in the 3 cases to be reported, but no microscopic description of these lesions is noted in the reported cases Although from the clinical descriptions the oral lesions seem to correspond to those in my cases, no pathologic report based on a biopsy from the

1 Hallopeau, H Sur une novelle forme de dermatite pustuleuse chronique en foyers a progression excentrique, Cong internat de dermat et de syph, 1889, p 344, Zweite Mittheilung uber Pyodermite vegetante (suppurative Form der Neumann'schen Krankheit), Arch f Dermat u Syph **45** 323, 1898, Pyodermite vegetante, ihre Beziehungen zur Dermatitis herpetiformis und dem Pemphigus vegetans, ibid **44** 289, 1898

2 Hartzel Dermatitis Vegetans, J Cutan Dis **19** 465, 1901

hyperkeratotic scaling of the plantar surface in Negroes, a condition which in white patients, except in rare instances, is due to Trichophyton rubrum

Cutaneous Moniliasis The relatively low incidence of cutaneous moniliasis may be explained by the age and sex of the subjects studied Only 13 cases were recorded 4 cases of tinea cruris, 2 of infection of the perineum and the perianal area, 1 of beefy tongue and 6 of intertrigo of the feet Ten of the 13 cases were of white persons Candida albicans was isolated from the "soft corn" intertriginous lesions of 2 Negroes In 1 Negro the organism was noted and isolated three times during a fourteen month period from an area of chronic tinea cruris with superficial moist scaling rather than the typical erythematous and exudative lesion

TABLE 3—*Incidence of Species Isolated in Cases of Dermatophytosis*

Total number of cases	429
Total number of cases in which cultures were yielded	214
Percentage of cultures isolated	47 55

	Dermatophytosis and Moniliasis		Dermatophytosis	
	Cases	Percentage	Cases	Percentage
T gypseum	127	59 3	127	63 2
T rubrum	70	32 7	70	34 8
E floccosum	4	1 9	4	2 0
C albicans	13	6 1	0	0 0
Total	214	100 0	201	100 0

Results of Culture In cases of dermatophytosis and moniliasis cultures yielded the organisms in 47 5 per cent of instances in which the slides were positive This percentage was even higher before an unfortunate siege with a contaminant, Monilia sitophila In addition, it was difficult to obtain cultures from infected nails and lesions of tinea cruris The dermatophytes were identified according to morphologic features, and C Albicans was identified by morphologic character and fermentation reactions

T gypseum was isolated in 59 3 per cent of the cases, T rubrum, in 32 7 per cent, Epidermophyton floccosum, in 2 per cent, and C albicans in 6 per cent In a strict sense, C albicans is not a dermatophyte In 9 of the 13 cases in which the yeastlike fungus was isolated it was not clinically possible to distinguish between dermatophytosis and moniliasis However, in order to satisfy the strict definition of dermatophytosis, percentages for the dermatophytes are given T gypseum, 63 2 per cent, T rubrum, 34 8 per cent, and E floccosum, 2 per cent

described a case with a protracted clinical course with skin and mouth lesions There were no biopsy reports of either the cutaneous or the oral lesions Wallhauser[9] described 2 cases, 1 with oral lesions, the clinical description of which closely corresponds to those of the 3 cases herein reported No biopsy findings of the oral lesions were reported A histologic description of the cutaneous lesions by Highman is given, and he concludes in this case that the process was that of a vegetating granuloma

In several cases reported, including those of Goldsmith,[4] Ledermann[10] and Pernet,[11] there were symptoms of chronic colitis Fischl[12] in 1922, in reporting his case of a *kleinpustulose vegetierende Dermatose,* indicated the extreme rarity of the disease and included a complete histologic study In this case there was an intermittent course of eight years, and for a short period, of a few weeks, the patient presented oral lesions on the buccal mucosa and tongue consisting of grouped pustules which responded to treatment promptly Three more cases recently reported by Conejo Mir, Conde and Calvente,[13] Finkler[14] and Cerruti[15] add no new information on this rare disease

REPORT OF CASES

CASE 1—P F, a 26 year old single woman, was presented at a clinic in oral medicine at Tufts Dental School in September 1944 with an oral disease which was undiagnosed at the time of presentation and remained so until the cutaneous complication in R B (case 2) illuminated the picture in each case so that a definite diagnosis of the oral condition was made in both cases

At the age of 2½ years the patient had an attack of pyelitis associated with high fever which lasted several days Recurrent attacks occurred until the age of 12, when the condition subsided and did not recur Five years ago the patient had purpura hemorrhagica involving both legs with associated articular symptoms These symptoms persisted for several weeks, after which recovery was complete Two years ago a cerebrospinal meningococcic meningitis was treated successfully with sulfadiazine, without any sequelae For the past three years she has had chronic diarrhea, intermittent in character and precipated by "nervous attacks"

9 Wallhauser, H J F Dermatitis Vegetans Report of Two Cases of the Hallopeau Type, Arch Dermat & Syph **19** 77 (Jan) 1929

10 Ledermann, R Ein Fall von Pyodermite vegétante, Berl klin Wchnschr **42** 146, 1905

11 Pernet, G Dermatitis Pustulosa Vegetans Recurrens, J Cutan & Genito-Urin Dis **30** 517, 1912

12 Fischl, F Ueber eine kleinpustulose vegetierende Dermatose, Arch f Dermat u Syph **139** 154, 1922

13 Conejo Mir, J, Conde, J M, and Calvente, D Pemphigus Vegetans (Neumann) of Type of Pyodermitis Vegetans (Hollopeau) Case, Actas dermosif **37** 509, 1946

14 Finkler, B Pyodermatitis Vegetans with Tumoral Aspect, Amatus **2** 679, 1943

15 Cerruti, H Chronic Pyodermitis, An brasil de dermat e sif **20** 9, 1945

although the presence of a lesion in the right axilla had been noted on his medical chart In fact, no cases with a service diagnosis of erythrasma were noted in the study

Black Hairy Tongue—One case of black hairy tongue was observed W C L, a white man aged 29, first noticed the infection in the fall of 1942, while in the South Pacific The disorder, treated unsuccessfully for three years, seemed to disappear spontaneously during a siege of seasickness on a troop ship returning to the United States in the fall of 1945 It recurred in October 1946 and was still persistent late in 1947 The papillae were slender, about ¼ inch (6 mm) in length and easily removed Although the patch on the tongue appeared black, the individual papillae were deep brown with a somewhat lighter base

Slides prepared from teased papillae revealed epithelial cells and a mass of fine hyphae, with budding yeastlike cells throughout Numerous attempts were made to culture the Nocardia-like organism, but only the species Candida tropicalis was grown

Aspergillosis of the Ear (Otomycosis) Examination was made of 41 patients, all white men, with service diagnoses of otomycosis For only 5 were fungi demonstrated The majority of the patients for whom fungi were not demonstrated showed erythema of various grades, exudative or dry, with crusted or scaling involvement of the concha In some of the cases the auditory canals were involved These cases were clinically either of seborrheic dermatitis with secondary bacterial invasion or of a primary infectious eczematoid dermatitis

From the 5 patients with otomycosis of the ear, species of Aspergillus were cultured Cultures from the 3 patients who had become infected in the United States all yielded Aspergillus niger Culture from a patient who had contracted the disease in the South Pacific yielded Aspergillus glaucus Culture from another patient, who had acquired the disease in Brazil, yielded Aspergillus versicolor Four of the patients exhibited moist macerated tissue, with the mycelium ramifying throughout, in 3 of these numerous conidiophores (and spore heads bearing conidia) also grew out from the wall of the auditory canal The cerumen of 1 patient showed dwarf conidiophores but normal-sized conidia (A glaucus) Cultures for the patient last mentioned, who had had the ear irrigated and cleaned just prior to the laboratory test, yielded only short fragments of mycelium

In addition, 4 patients with generalized dermatophytosis showed chronic hyperkeratotic scaling of the concha of the ear, from 3 of these patients T rubrum was isolated, and from 1, T gypseum

An unusual case of otomycosis of the ear canal and concha of the right ear due to T rubrum was noted in a veteran after the completion of the survey A report follows

A man aged 25 had noticed scaling of the feet since childhood, but he stated that the right hand and ear had become involved while he was stationed in Burma in 1945 Potassium hydroxide mounts revealed mycelium in scales removed from

and smearing the contents revealed polymorphonuclear leukocytes, 30 per cent of which showed coarse eosinophilic granules (fig 2) This recurrence, in which the primary lesions of the disease were in the mouth, caused very mild subjective clinical symptoms The patient was advised that the recurrence might involve the whole mouth, and she considered giving up her employment as a secretary in order to build up her resistance

The patient was seen in November 1948, and at that time the mouth had been free from lesions and she had had good health for eighteen months

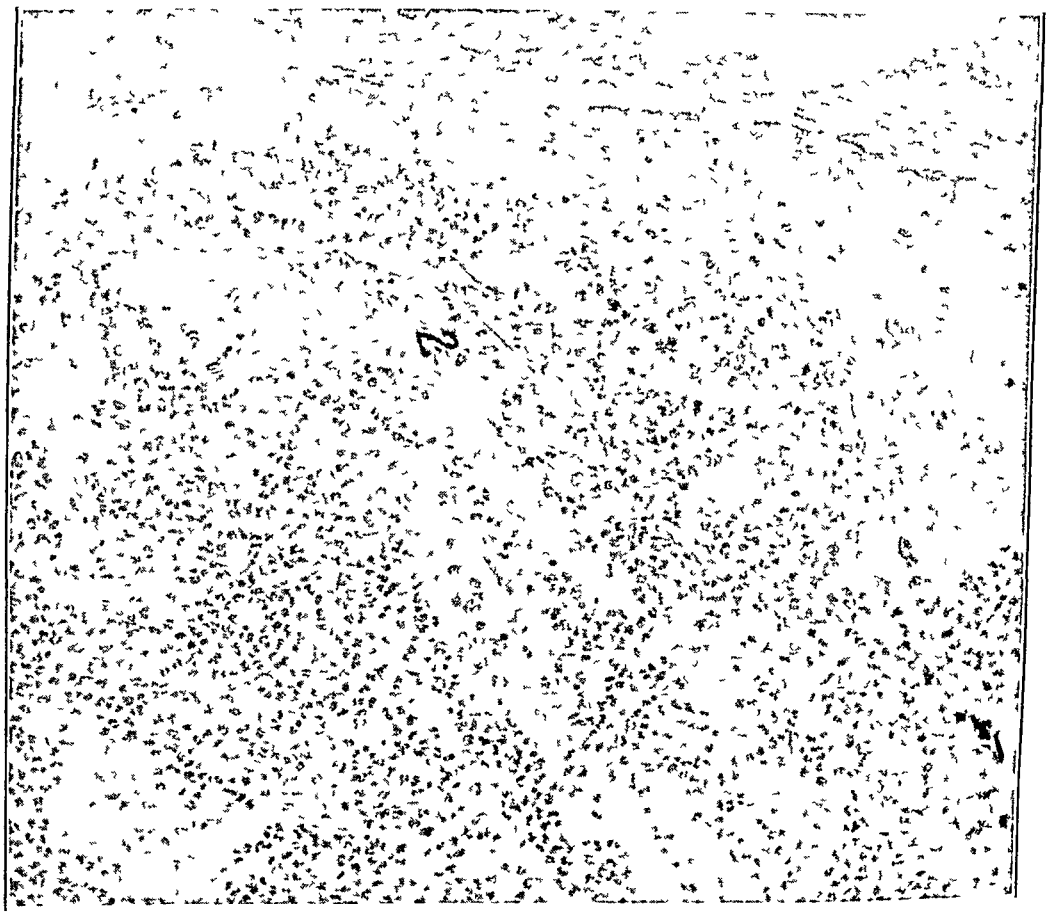


Fig 1 (case 1) —Granulomatous reaction of the buccal mucosa, the eosinophil is the predominant cell

Case 2—R B, a 47 year old white man, was presented at the meeting of the New England Dermatological Society in October 1944[16] and again in February 1946, at a meeting of the Atlantic Dermatological Conference[17]

Except when incapacitated by chronic colitis of the spastic type, the patient has continued as an office worker for the past twenty years In 1920 he was treated at the Massachusetts General Hospital for three months for colitis A

16 McCarthy, F P Case of Stomatitis, Arch Dermat & Syph **53** 186 (Feb) 1946

17 McCarthy, F P Dermatitis Vegetans of Mouth, Arch Dermat & Syph **57** 598 (March) 1948

SUMMARY

1 No new strains or species of superficial parasitic fungi were noted in a study of 1,000 veterans with a service diagnosis of mycosis

2 Of the 466 patients for whom laboratory findings were positive, dermatophytosis was recorded for 87 1 per cent, moniliasis, for 3 per cent, tinea versicolor, for 8 4 per cent, otomycosis (aspergillosis of the ear), for 1 1 per cent, and black, hairy tongue and erythrasma, for 0 2 per cent each.

3 The ratio of positive to negative cases (and areas) amply reveals the inclination to designate most vesicular and exudative lesions of the hands and feet as mycotic in origin

4 There were 48 cases of tinea manus, in the majority of which the disease was of the chronic hyperkeratotic scaling type Fewer cases were seen of tinea pedis with dermatophytids than of tinea pedis with tinea manus

5 Cultures yielded dermatophyte in 47 5 per cent of the cases in which slides were positive The incidence according to cases was as follows T gypseum, 59 3 per cent, T rubrum, 32 7 per cent; E floccosum, 2 per cent, and C albicans, 6 per cent According to isolations from various clinical sites of dermatophytosis, the incidence of T gypseum decreased and the incidence of T rubrum increased, indicating that T rubrum causes generalized dermatophytosis oftener than does T gypseum

6 Species of Aspergillus were cultured from the 5 proved cases of otomycosis

Harvard University

Veterans Administration Regional Office, 1031 South Broadway

peripheral blood eosinophilia Six sulfathiazole tablets daily for two weeks had no effect on the oral lesions, which had appeared prior to the use of the sulfathiazole medication

The patient was first seen by me in June 1944 with an unusual type of stomatitis which presented a condition I had not previously seen in the mouth, except for the oral lesions seen in case 1

There was a generalized eruption of the mucous membrane which was characterized by an edematous, exuberant buccal mucosa thrown into folds, especially pronounced in the vestibule, and on the gingiva with some involvement of the hard and soft palates and the tonsillar regions The upper jaw was edentulous, and there were only eight remaining lower teeth (later extracted, in October 1945) The oral lesions showed miliary abscesses which made the lesions particu-

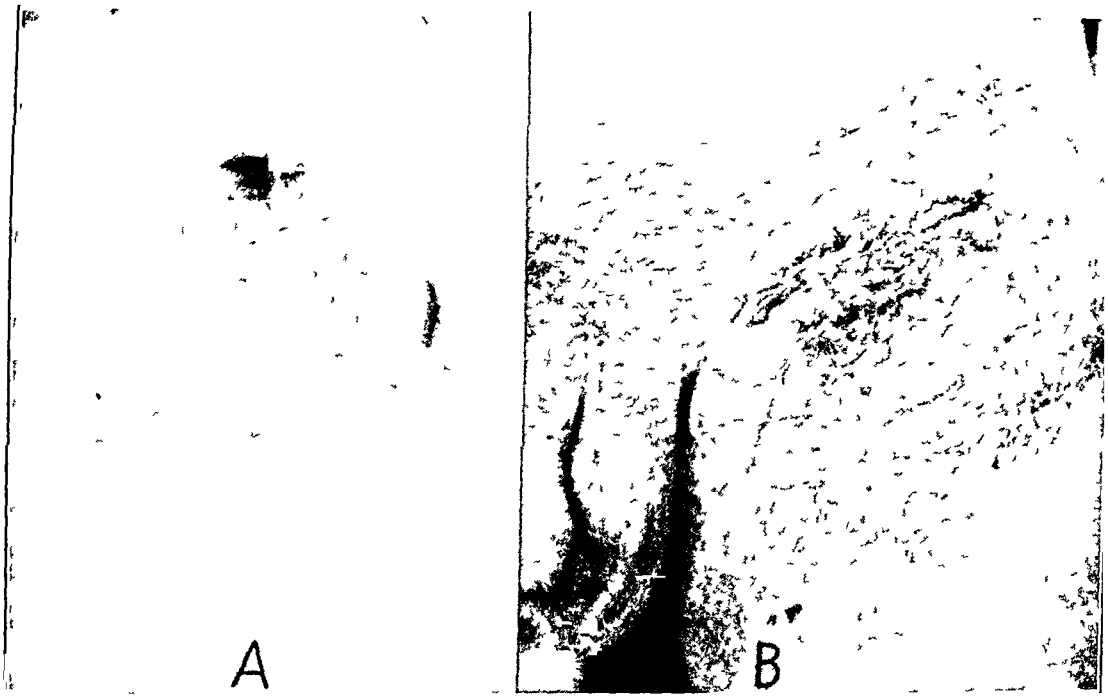


Fig 3 (case 2) —*A*, residual microabscesses with exudate on the palate, the rupture of the abscesses was due to pressure of the upper dentures *B*, dermatitis vegetans of the left groin complicating the primary oral involvement

larly distinctive Under the upper plate a mucoid fibrinopurulent exudate was present, associated with the rupture of these miliary abscesses (fig 3*A*)

The patient was treated up to January 1945 with local soothing alkaline washes and 2 per cent aqueous solution of methylrosaniline chloride topically applied to the oral lesions Three tablets of feosol® (ferrous sulfate) daily and 6 capsules of polytaxin® (each containing 10,000 U S P units of vitamin A, 0 45 mg of thiamine hydrochloride, 50 mg of riboflavin, 25 mg of ascorbic acid and 1,000 U S P units of crystalline vitamin D from ergosterol) were taken daily for a period of about six months A moderate improvement in the oral condition occurred, especially while the patient ceased work for a few months

In April 1945 the patient reported at the office again with a complication which began three months previously The history as given by the patient was

oral lesions has been included in Hallopeau's cases or in those cases reported by subsequent investigators There has not been a single case of pyostomatitis vegetans described as an entity in the literature, and only in 2 of Hallopeau's cases and 2 others were there oral lesions which one could call typical of the lesions described in my cases In the 35 cases so far described in the literature only 7 showed oral lesions, of which 4 showed the classic picture of a vegetating mucosa with microabscesses

In addition to the group of cases described as occurring in adults, there are cases reported in children which conform to the clinical description of the disease, in none of these were there intraoral lesions Wende and DeGroat [3] described 10 such cases, all occurring in children under 1 year of age

Hallopeau in his earliest reports of 5 cases regarded the disease as a clinical entity, but later he described it as a form of pemphigus vegetans There is a more or less general agreement in the reports of subsequent observers that pyodermatitis vegetans in some of its manifestations may simulate pemphigus vegetans but remains as a clinical entity

Hallopeau's description of oral lesions in 2 of his cases, together with the description of the oral lesions in 1 of Goldsmith's cases, fits the characteristic lesions found in my cases The cutaneous lesions dominated the clinical picture in the cases reported, and the oral lesions are referred to as a part of the clinical findings

Fordyce and Gottheil [5] discussed the relation between dermatitis vegetans and dermatitis herpetiformis and described the pathologic picture of the disease in reporting 1 case Hartzell reported a case in which there were vegetations in the groin and the patient died a few weeks after admission to the hospital No oral lesions occurred in his case Wickham,[6] in 1891, described a case resembling Hallopeau's original case, which the latter called *dermatite pustuleuse chronique en foyers à progression excentrique* Pusey [7] reported 2 cases of vegetating dermatoses without oral lesions P King-Smith,[8] in 1910,

3 Wende, G, and DeGroat, N K Dermatitis in Infants Report of Two Cases, J Cutan Dis **29** 473, 1911

4 Goldsmith, W N A Case of Pyodermite Végetante (Hallopeau), Brit J Dermat **53** 299, 1941

5 Fordyce, J H, and Gottheil, W S Dermatitis Vegetans in Its Relation to Dermatitis Herpetiformis, J Cutan Dis **24** 543, 1906

6 Wickham Une cas rare de dermatite herpetiforme de Duhring varieté pustuleuse et vegetante, Ann de dermat et syph **11** 1005, 1891

7 Pusey, W A Vegetating Dermatoses, with Report of Two Cases, J Cutan Dis **24** 555, 1906

8 King-Smith, P A Case of Dermatitis Vegetans, J Cutan Dis **28** 605, 1910

discharge from the back of his throat, which caused no discomfort About three months later the condition recurred and has persisted to the present time with exacerbations and remissions but never entirely clearing up The family physician treated him with paints and gargles, with little relief for five to six years However, there was little or no discomfort associated with this condition The last year after he was treated by his family doctor it became uncomfortable The roof of the mouth and mucous membranes began to get dry, cracked and burning He visited many local physicians and a specialist without any change in the condition Lately the condition has been getting worse, and when seen by

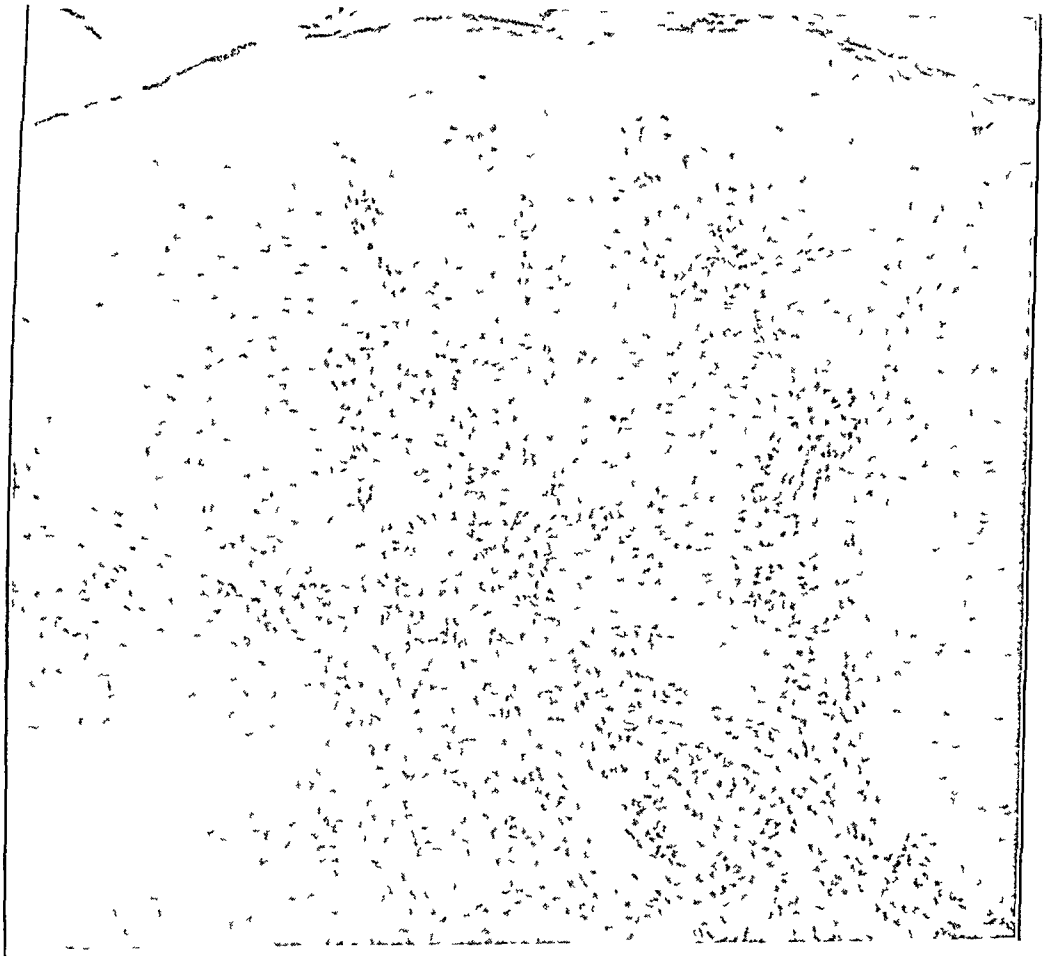


Fig 4 (case 2) —Section from biopsy specimen from the vegetating cutaneous lesion of the groin, showing the granulomatous reaction with infiltration of eosinophils

me it involved his throat, the roof of his mouth, and the mucous membranes of his cheeks A rash on his chest and back had persisted for years but had caused very little discomfort

The physical examination of the patient revealed essentially normal conditions except for the oral condition and the cutaneous eruption which was diagnosed as tinea versicolor The laboratory data were not significant

The following descriptions of the oral condition are noted on the hospital record

The patient has been below par for the past few years and has been treated for anemia by her private physician

In February 1944 appeared what the patient thought was a "canker sore" on the buccal mucosa near the right external commissure, this spread within a few weeks to involve the greater part of the mouth, including the vestibule, mucosa of both cheeks, hard and soft palates and gums The patient was treated by her family physician and dentist with various mouthwashes without any results The oral lesions caused very little discomfort and did not interfere with eating Sulfadiazine locally and by mouth, prescribed by the family physician, had no effect on the lesions

I saw the patient for the first time in May 1944, when the oral cavity showed a generalized eruption involving particularly the mucous membrane of both cheeks, the vestibule of the mouth, the gums and the palate The lesion was characterized by soft hypertrophic folds studded with miliary abscesses from pinpoint to pinhead size with superficial areas of necrosis The verrucous mucous membrane was red and soft and not tender to the touch There were a few carious teeth, but otherwise the teeth were in good condition

No definite diagnosis was made, as the lesions did not resemble any eruptive oral condition seen by me Lupus erythematosus, stomatitis due to fungus infection and oral pemphigus were considered

A biopsy specimen showed acanthosis with focal necrosis of the epithelial layer There was a marked cellular infiltration of the tunica propria with the eosinophil as the predominating cell (fig 1)

In spite of various forms of local treatment, including gold and sodium thiosulfate N F, 0 050 Gm for four treatments, no results were obtained in controlling the condition The local treatment consisted of alkaline mouthwash, 2 per cent aqueous solution of methylrosaniline chloride (gentian violet) and isotonic sodium chloride solution Internally iron, multivitamin preparations and, later, liver and iron administered parenterally were used The patient was admitted to the hospital in July and given 120,000 to 150,000 units of penicillin intramuscularly for five days without any improvement in the oral condition

Culture from the lesions in the oral cavity showed the usual bacterial flora without any distinctive predominating organisms In the culture from the miliary abscesses Staphylococcus aureus predominated

In December 1944, after extraction of four teeth and at the end of a prolonged vacation, the patient showed some improvement in the oral lesions The soft verrucous elevations of the buccal mucosa of both cheeks were definitely flattened, but the palate showed the persistent eruption characterized by the miliary abscesses The patient showed no great change in weight, 140 pounds (63 5 Kg), but there was improvement in the diarrheal condition Examination of the blood showed an eosinophil count of 18 per cent The patient experienced but slight discomfort from the oral disease, and her appetite was good

A prolonged vacation in the spring of 1945, together with injections of liver and iron preparations given by her family physician, resulted in continued improvement of the oral lesions, although remissions were noted, when the oral eruption became worse, with verrucous lesions and miliary abscesses

From April to September 1945 the mouth showed a gradual improvement, and early in September all lesions had disappeared and the mucous membrane appeared normal At no time did cutaneous lesions develop The mouth remained normal until the middle of November 1945, when a slight irritation developed in the lower third molar region Examination showed a cluster of miliary yellowish lesions on a swollen reddened inflammatory base Puncturing these lesions

"virus" pneumonia developed in April 1944, which was followed by a febrile period of about three months' duration He was subject to chills and fever (temperatures of 99 to 101 F) with weakness and a loss of weight during this period Various laboratory tests and physical examinations did not clarify the diagnosis The patient was treated with sulfathiazole during the few days of the pneumonia attack and received two 7½ grain (0 5 Gm) tablets daily for a period of about three months

The patient stated that the oral eruption began promptly, probably within a few days, after the onset of the pneumonia, under the upper dental plate in the



Fig 2 (case 1)—Section from an oral miliary epidermal abscess, note the eosinophilic cellular content

hard palate region This oral process gradually spread to involve the entire buccal cavity The oral condition was treated by his family physician and dentist with various mouthwashes and local applications including sodium perborate, neoarsphenamine, methylrosaniline chloride, hydrogen peroxide, S T 37 (1 1,000 solution of hexylresorcinol in glycerin and water), tincture of iodine, ultraviolet radiation and alkaline mouthwashes, without any improvement The patient experienced only a mild sore mouth and in the morning had a bad taste with an accumulation of a mucoid pseudomembrane especially pronounced on the hard palate All laboratory tests failed to disclose anything significant except a

as follows Early in January a "pimple" developed in the groin, it was the size of the head of a pin, but it grew to resemble a "ringworm" The outer fringe of the ring grew larger slowly, and a raised center "puffed up like a wart" The lesion was treated by the family doctor with ammoniated mercury ointment, iodex® ointment, sulfathiazole powder and injections of penicillin, 100,000 units every three hours for four days, without any effect on the lesion In April the lesion spread rapidly, and on April 24, when I saw the lesion, it covered an extensive area in the groin and upper part of the thigh, 10 cm in diameter and raised above the skin surface up to 2 cm The appearance suggested blastomycosis cutis (fig 3 *B*), and the patient was promptly hospitalized The oral lesions were somewhat improved over the condition in December 1944, but the palate showed activity with verrucous lesions studded with miliary abscesses

A biopsy of the cutaneous lesion and a second biopsy of the oral lesions showed almost identical pictures A section from the oral cavity showed pronounced hyperkeratosis and acanthosis with a verrucous appearance with invaginations and miliary abscesses of the epidermis and tunica propria containing eosinophil and neutrophil polymorphonuclear leukocytes There was edema of the tunica propria with a deep infiltration with eosinophils and polymorphonuclear leukocytes and lymphoid and plasma cells There was a definite increase in capillary blood vessels, and the whole picture suggested a granuloma A section from the skin showed essentially the same picture except that the invaginations were deeper with keratinized epithelium on the surface The cellular infiltration showed the eosinophil to be the predominating cell with a very deep infiltration into the cutis (fig 4) Blastomycetes were not demonstrated The cultures from the cutaneous lesions showed Staph aureus with a few hemolytic streptococci

A small crusted verrucous lesion appeared on the neck over the thyroid cartilage and a few small crusted lesions occurred in the scalp The use of 2 per cent aqueous solution of methylrosaniline chloride and ammoniated mercury ointment together with potassium permanganate (1 10,000) soaks caused a marked improvement in the skin eruption On discharge from the hospital after three weeks he received five roentgen ray treatments to a total dose of 300 r (0 2 mm aluminum filter) Early in August the cutaneous lesions were entirely healed, leaving a pigmented area in the left groin The oral lesions still persisted with a residual miliary pustular eruption on a swollen bright red edematous base involving principally the mucosa over the hard and soft palates Local treatments to the mouth included benzalkonium chloride (zephiran chloride®), methylrosaniline chloride and four doses of 50 r each (0 2 mm aluminum filter) to the palate at weekly intervals No visible effect was noted from the local therapy plus vitamins and iron and liver preparations by mouth The remaining eight lower teeth were removed in October 1945

Case 3—W D M, a 33 year old man, was seen by me in consultation at the Joseph H Pratt Diagnostic Hospital in June 1946

The patient worked as a laborer in the paper mills Except for an attack of measles in childhood, he had had no other diseases At the age of 16 he had an eruption of blisters on his feet which cleared up in about one month There is a history of hives, usually extremely evanescent, after exposure to a "cold draft" and not especially related to food intake

The patient smoked about 30 cigarets daily which aggravated his mouth condition The use of liquor made his mouth worse, and so he did not drink

The patient was well until 1936, at which time an oral disease, which was diagnosed as trench mouth, developed while he was in a Civilian Conservation Camp It was painted and cleared up in about five days There was a white